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RHEUMATOLOGY



MOWAFY

INTERNAL MEDICINE

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In Capsule Series
Internal medicine

Rheumatology

Dr. Ahmed Mowafy

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

لَا يَكْفُ اللَّهُ نَفْسًا إِلَّا وُسْعَهَا لَهَا مَا كَسَبَتْ وَعَلَيْهَا مَا اكْتَسَبَتْ رَبَّنَا لَا تُؤَاخِذْنَا إِنْ
نَسِينَا أَوْ أَخْطَأْنَا رَبَّنَا وَلَا تَحْمِلْ عَلَيْنَا إِكْرًا كَمَا حَمَلْتَهُ عَلَى الَّذِينَ مِنْ قَبْلِنَا رَبَّنَا وَلَا
تُحَمِّلْنَا مَا لَا طَاقَةَ لَنَا بِهِ وَاعْفُ عَنَّا وَارْحَمْنَا أَنْتَ مَوْلَانَا فَانصُرْنَا عَلَى
الْقَوْمِ الْكَافِرِينَ

صدق الله العظيم

سورة البقرة (آية 286)

Preface

- *First and foremost, thanks are due to **ALLAH**, to whom I relate any success in achieving any work in my life.*
- *Great thanks to those who helped me, and greater thanks to those who try to break my wings as they make me more able to fly.*
- *My thanks are extended to all my medical students whom I produce this series "**In Capsule Series**" to obtain a higher degree in internal medicine by a simple effort.*
- *Finally, I wish to thank all members of My Family, my colleagues , my Friends and even all my patients for their continuous help, encouragement and support.*

Ahmed Mowafy

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RHEUMATOLOGY SCHEME

Definition :

(of any rheumatic disease)

It's a connective tissue disorder characterized by articular & extra-articular manifestations, most probably autoimmune.

Etiology :

(of any rheumatic disease)

- Still questionable.
- **But** , most probably autoimmune.
- Genetic factors may play a role (+ve family history & HLA association).
- Environmental factors play some role.
- In SLE, add :
 - Hormonal factor also may play an important role.
 - Drug induced lupus : **Hydralazine, INH, penicillamine, phenytoin.**

Clinical Picture :

(of any rheumatic disease)

- ♀ > ♂ ☺

(Exceptions : Gout, Polyarteritis nodosa, Ankylosing spondylitis ...)

- Rheumatoid Arthritis : ♀ : ♂ = 3:1
- SLE : ♀ : ♂ = 9:1 ☺

I. General manifestations.

II. Articular manifestations.

III. Extra-articular manifestations.

I. General manifestations:

- Fever.
- Fatigue.
- Weight loss.

II- Articular manifestations:

(3D)

- Distribution .
- Description .
- Deformity .

Distribution:

1- **Number of the affected Joints** : mono or poly arthritis e.g.

- RA, SLE, chronic gout ⇒ polyarthropathy.
- Acute gout, septic arthritis ⇒ monoarthropathy.
- RA may be monoarthropathy in atypical form.

2- **Symmetrical or asymmetrical** :

All are asymmetrical except Rheumatoid Arthritis & SLE – both are symmetrical.

3- **Small Joints or large Joints** : RA & SLE → small Joints.

4- **Peripheral** (upper & lower limbs) **or central** (vertebral column & sacroiliac) :

RA & SLE : peripheral > central .

5- **Erosive or non erosive**:

- Non erosive : inflammation of synovial membrane only.
- Erosive : erode & destroy the cartilage e.g. RA, chronic gout, septic arthritis. ☠

Description:

- | | | |
|------------|----------------------------|---------------|
| 1- Hotness | 2- redness | 3- Tenderness |
| 4- Swollen | 5- Limitation of movement. | |

Deformity:

If the lesion is erosive only.

e.g.: Rheumatoid arthritis → (see later)

PLEASE, DON'T FORGET THIS FACT : 😊

Articular manifestations of rheumatoid arthritis = 3 x

III- Extra articular manifestations:

The same in any Rheumatologic disease, **Except** as regard to **skin & Renal** manifestations.

1- Skin manifestations:

- ♣ RA: Palmer erythema, SC nodule.
- ♣ SLE : 6 (*see later*)
- ♣ Scleroderma : edema, **Skin induraion** then pigmentation.
- ♣ In all diseases : pallor, vasculitis , Raynaud's phenomenon.

2- Renal manifestations:

- ♣ RA : Amyloidosis.
- ♣ SLE: Glomerulonephritis (Lupus nephritis)
- ♣ Scleroderma : Scleroderma renal crisis (*see later*)

3- Cardiac manifestations:

- ♣ Pericarditis.
- ♣ Myocarditis.
- ♣ Endocarditis (?)
- ♣ Systemic Hypertension
- ♣ Ischemic heart diseases.

4- Chest manifestations:

- ♣ Pleurisy.
- ♣ Interstitial pulmonary fibrosis.
- ♣ Pulmonary infarction
- ♣ Pulmonary Hypertension.
- ♣ **Caplan's syndrome** in RA.
- ♣ ARDS in SLE .

5- CNS manifestations:

- ♣ Psychosis.
- ♣ Depression.
- ♣ Chorea.
- ♣ Epilepsy.
- ♣ Neuropathy.
- ♣ Myopathy.
- ♣ Cerebral vasculitis → stroke.

In RA, add : Carpal tunnel syndrome & paraplegia.

6- Eye manifestations:

- ♣ Conjunctivitis.
- ♣ Scleritis.
- ♣ Anterior uveitis. (NOT in rheumatoid arthritis) MCQ

7- GIT manifestations:

- ♣ Nausea & Vomiting .
- ♣ Esophagitis.
- ♣ Abdominal pain due to vasculitis.
- ♣ Gastritis & peptic ulcer
- ♣ Pancreatitis .
- ♣ Hepatosplenomegaly.
- ♣ **Dysphagia**, malabsorption syndrome & constipation in **scleroderma**.

8- Blood manifestations:

♣ **Anemia :**

- ☉ Normocytic normochromic : autoimmune hemolytic anemia .
- ☉ Microcytic hypochromic :
 - Anemia of chronic disease.
 - Iron deficiency anemia : due to chronic blood loss.

Investigations :

- 1- x-ray :**
- ☺ Osteoporosis.
 - ☺ In erosive diseases:
 - Narrow joint space .
 - Deformity. (mention)
 - ☺ x-ray chest: Pleural effusion.

2- Aspiration of synovial fluid : Antibodies.

Disease	WBCs / mm ³	Crystals / polarized light microscopy
Normal	< 200	-ve
Non- inflammatory	< 2000	-ve
Rheumatoid arthritis	5000 - 50000	-ve
Gout	5000 - 50000	○ Needle shaped crystals of Na urate. ○ -ve birefringent.
Pseudogout	5000 - 50000	Rhomboid, +ve birefringent crystals of Ca pyrophosphate.
Septic arthritis	> 50000	-ve

3- Blood picture :

- Anemia: ↓↓ RBCs : normocytic or microcytic.
- WBCs: ↑↑ except in SLE & Felty's syndrome. MCQ
- ESR: ↑↑
- CRP: ↑↑ except in SLE . (CRP may ↑↑ in SLE with infection)
- SGOT & SGPT : ↑ , this is more likely to be drug induced rather than a result of the disease process.

4- Serological tests:**➤ Non specific Antibodies:**

(may be +ve in all rheumatologic diseases , inflammation or even in normal population)

I- Rheumatoid Factor (RF):

- +ve in 70% of RA
- +ve in 25% of SLE & scleroderma.
- Highest incidence of rheumatoid factor is found in : Sjögren's syndrome. (90%) MCQ

II- Lupus Erythematosus (LE):

- +ve in 80% of SLE.
- +ve in 20% of RA.

III- Antinuclear antibody (ANA):

- +ve in 95-100% of SLE (most sensitive)
- +ve in 90% of scleroderma.
- +ve in 30% of RA.

➤ Specific Antibodies :

- **Anti CCP** (Cyclic Citrullinated Peptide, NOT ContraCeptive Pills) ⇒ Rheumatoid arthritis. 😊
- **Anti double stranded DNA(dsDNA)** ⇒ SLE. (80%)
- **Anti-sm** (Anti-smith Ab, **NOT** anti smooth muscle Ab) ⇒ specific to SLE.
- **Anti Ro Anti La** ⇒ specific to SLE , Sjogren's syndrome. 🎵 🎵
- **Anti histone antibody:** ⇒ drug induced SLE e.g. hydralazine.
- **SCL 70 antibody** ⇒ scleroderma.
- **Anti- centromere** ⇒ CREST syndrome.
- **Anti-RNP** (ribonucleoprotein) : associated with mixed connective tissue disease.
- **cANCA** (Anti-Neutrophil Cytoplasmic Ab) ⇒ Wegener granulomatosis (90%)

➤ Complement :

Low complement levels indicate consumption as in active SLE.

Differential diagnosis :

- ✎ DD of Polyarthropathy. *See later*
- ✎ DD of monoarthropathy. *See later*

Treatment :

I. General : Rest, Physiotherapy.

II. Medical :

- ✎ **Cortisone.**
- ✎ NSAIDs .
- ✎ DMARDs : Gold, Penicillamine
- ✎ Immunosuppressive drugs : (methotrexate , cyclophosphamide)

III. Treatment of complications : e.g.

- End stage kidney damage in a cases of SLE : dialysis or kidney transplant.
- Renal crisis in a cases of scleroderma : ACE inhibitor is the drug of choice " Life saving "

The best advice I ever heard is, don't take anyone else's advice

RHEUMATOID ARTHRITIS

Definition :

- It's a chronic systemic inflammatory disease characterized by articular & extra articular manifestations, most probably autoimmune.
- RA is the most common form of inflammatory arthritis. (1-3% of the population)

Etiology : Still questionable, but many theories are suggested :

- Autoimmunity : Infiltration of synovial membrane with lymphocytes.
- Genetic factor may play a role : +ve family history, HLA association (HLADr4)
- Environmental factor : e.g. infection mostly viruses.

Pathology :**I- Articular :**

1. Synovitis: Thick, inflamed & infiltrated with lymphocytes & plasma cells.
2. Pannus formation: erode & destroy the articular cartilage.
3. Cartilage is eroded & destroyed → subluxation & deformity.

The predominant infiltrating cell is T lymphocyte. So, disease like HIV, in which T cells are decreased, will improve pre-existing RA. This is the reason why RA is very rare in patients with HIV.

II- Extra-articular :

SC. Rheumatoid nodules : In 20% of RA.

- Central fibrinoid degeneration with inflammatory cells covered by fibrous capsule.
- Exclusive in sero+ve patient.

Mode of onset :

- ◆ Gradual onset (*months*) : 70 %
- ◆ Intermediate onset (*weeks*) : 20 %
- ◆ Acute onset (*days*) : 10 %

NB : Typical onset is gradual polyarthritis but may begin with monoarthritis.

Clinical Picture: - 1-3% of population - ♀ > ♂ (3:1) ☺

I. General:

- Fever. - Fatigue - Weight loss.
- **Morning stiffness** : lasting for 1 hour or more.

II- Articular manifestations: 3D 3 × 5

Distribution:



- 1- Polyarthropathy .
- 2- Symmetrical .
- 3- It affects mainly the peripheral Joints (UL, LL) > central joints .
- 4- Affects mainly small Joints e.g.: hands, feet (proximal interphalangeal, metacarpophalangeal & wrist Joints).

N.B: **The distal interphalangeal Joints** are usually spared.

- 5- The arthropathy is erosive ⇒ deformity.

Description:



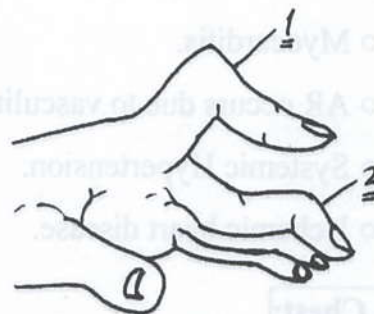
- 1- Redness 2- Hotness 3- Tenderness
- 4- Swollen 5- Limitation of movement.

Deformity:



1- Hand deformity:

- 1- *Boutonniere deformity*: extended distal & flexed proximal interphalangeal Joint.
- 2- *Swan-neck*: flexed distal & extended proximal interphalangeal Joint.
- 3- Ulnar deviation of metacarpophalangeal Joint.
- 4- *Z-shaped thumb*: flexed metacarpo-phalangeal & extended interphalangeal joints.
- 5- Carpal tunnel syndrome.
- 6- Telescope deformity: due to substantial absorption of metacarpal and phalangeal bone ends. Involved fingers may be extended or shortened as the telescope.



- 2- **Cricoarytenoid**: stridor & hoarseness of voice.
- 3- **Atlanto-axial subluxation**: Spinal cord compression $\Rightarrow$ paraplegia.
- 4- **Tendon rupture**: (extensor more than flexor) e.g.: flexion of hip & knee.
- 5- **Synovial membrane rupture** : Baker cyst (popliteal cyst) .

III- Extra-articular manifestations :

i- Skin:

- S.C. rheumatoid nodules.
- Palmer erythema.
- Vasculitis.
- Pallor.

ii- Renal:

- Amyloidosis.
- Glomerulonephritis: drug induced e.g.: NSAIDs, Gold & Penicillamine.

iii- Cardiac:

- Pericarditis (30%).
- Myocarditis.
- AR occurs due to vasculitis.
- Systemic Hypertension.
- Ischemic heart disease.

Causes of edema LL in RA :

- Nephrotic syndrome (due to amyloidosis or drug induced GN).
- Pulmonary Hypertension or IPF $\rightarrow$ cor pulmonale
- Myocarditis $\rightarrow$ HF.

iv. Chest:

- Pleurisy & pleural effusion.
- Interstitial pulmonary Fibrosis.
- Pulmonary Infarction.
- Pulmonary Hypertension.
- **Caplan's syndrome** : rheumatoid Nodules with pneumoconiosis. (rare).
- **Methotrexate** $\rightarrow$ **pneumonitis**.

Rheumatoid pleural effusion :

- Pleural fluid glucose < 30 mg%
- Cholesterol crystals.
- Secondary empyema common.

MCQ

V. CNS:

- **Carpal tunnel syndrome:** compression of the median nerve due to hypertrophied synovium, it may be the first symptom of R.A.
- **Atlanto-axial subluxation** ⇒ spinal cord compression ⇒ paraplegia.
- Psychosis.
- Depression.
- Neuropathy.
- Myopathy.
- Chorea.
- Epilepsy.
- Cerebral vasculitis ⇒ stroke .

vi. Eye:

- Conjunctivitis
- **Scleritis** ⇒ repeated attack ⇒ scleromalacia (blue sclera).
- Iritis is not common.

vii- GIT:

- Nausea & vomiting.
- Abdominal Pain due to vasculitis.
- Hepatosplenomegaly.
- Pancreatitis.
- Gastritis & peptic ulcer.

viii- Blood:

- Anemia :
 - Normocytic normochromic anemia. (Autoimmune hemolytic anemia).
 - Microcytic hypochromic anemia (Iron deficiency, anemia of chronic disease)

Rheumatic fever	Rheumatoid arthritis
- < 6 weeks	- Chronic disease > 6 weeks
- Large Joints	- Small Joints
- Not erosive	- erosive

Investigations : Just scheme

1- X-ray :

- None of the X-ray finding is diagnostic
- Osteoporosis.
- Narrow Joint space.
- Deformity (*mention*)
- Loss of articular cartilage and bone erosions develop after months of sustained activity.
- X-ray chest: Pleural effusion.



2- Aspiration of synovial fluid : Antibodies.

3- Blood :

- ↓↓ RBCs: Anemia (normochromic – hypochromic)
- WBCs: ↑↑ (↓↓ in felty's syndrome)
- ESR : ↑↑↑ may > 100 in severe cases.
- CRP: ↑↑

4- Serological tests:

- RF : +ve in 70% of cases.
- LE : +ve in 20% of cases.
- ANA : +ve in 20% of cases.
- Recently : **Anti CCP** (cyclic citrullinated peptide NOT contraceptive pills). ☺

Rheumatoid Factor : It's an IgM against changed IgG.



- It may be +ve in :

- Normal population (4%) , 25% of the elderly.
- Rheumatic conditions: Sjogran's syndrome, RA, SLE, Scleroderma, Dermatomyositis...
- Non rheumatic conditions: Infective endocarditis , Myeloma , TB , HCV , Syphilis

Value of RF in RA :

- Help in diagnosis (not sure alone).
- Help in prognosis (follow up).

1987 ACR classification criteria for Rheumatoid arthritis:

Patients can be said to have RA if they have at least 4 of the following **7** criteria :

- 1- Morning stiffness > 1h
- 2- Arthritis of 3 or more joints.
- 3- Arthritis of hand joints.
- 4- Symmetrical arthritis.
- 5- SC Rheumatoid nodules.
- 6- Characteristic x-ray finding e.g. erosions.
- 7- +ve Rheumatoid factor.

ACR : American College of Rheumatology

Criteria 1, 2, 3 & 4 must be present for at least 6 weeks

2010 ACR/EULAR Classification Criteria for Rheumatoid Arthritis :

➡ Definite RA= ≥ 6

➡ Patients with a score <6 should be assessed over time

	Score
Joint involvement : 0-5 (Any swollen or tender joint excluding DIP, 1 st MTP, 1 st CMC)	
○ 1 large joint (shoulders, elbows, hips, knees, ankles)	0
○ 2-10 large joints	1
○ 1-3 small joints e.g. MCP, PIP, MTP 2-5, thumb IP, wrist (large joints not counted)	2
○ 4-10 small joints (large joints not counted)	3
○ >10 joints (at least one small joint) e.g. temporomandibular, sternoclavicular,...	5
Serology : 0-3	
○ Negative RF <u>AND</u> negative ACPA	0
○ Low positive RF <u>OR</u> low positive ACCP	2
○ High positive RF <u>OR</u> high positive ACCP (> 3 times the upper limit of normal)	3
Acute phase reactants : 0-1	
○ Normal CRP <u>AND</u> normal ESR	0
○ Abnormal CRP <u>OR</u> abnormal ESR	1
Symptom duration : 0-1	
○ < 6 weeks	0
○ ≥ 6 weeks	1

Factors associated with poorer prognosis :

- Male Patients
- Insidious polyarticular onset
- Extra articular manifestations
- Functional disability at one year after start of the disease
- High value of RF
- Presence of HLADR4
- Radiographic evidence of erosions within 3 years of onset of disease.

Treatment of RA:

The **cornerstone** strategy for management of RA is induction of remission early before structural damage.

(A) General treatment :

1. Rest :

- Complete bed rest is advisable in active disease.
- Articular rest by the use of splints will help to suppress synovitis in isolated joint inflammation.

2. physiotherapy :

- It can be started when the acute phase disappears.
- Rehabilitation program helps in education of patients, minimizing pain & swelling by the use of local heat, cold & electrotherapy.
- Passive & active exercise program aims at strengthening muscles to preserve range of motion and minimizing deformity.

(B) Medical treatment:

1- **NSAIDs** : for relieve of pain & inflammation (*symptom-modifying*).

- *Aspirin* 500 mg/ 4h
- *Diclofenac* 50mg t.d.s.
- *Paracetamol* 500mg t.d.s.
- *Indomethacin* 50 mg t.d.s.
- *Ketoprufen* 100mg t.d.s.
- *Celecoxib* (*Celebrex*), *Lornoxicam* (*Xefo*) : COX-2 inhibitors.

Mechanism : cyclooxygenase inhibitor (COX-1 & COX-2 inhibitors)

Side effects : *mnemonic* : ASPRIN

- **A**plastic anemia.
- **S**alt & water retention leading to edema & worsening of hypertension & heart failure.
- **P**eptic ulcer : specially with COX-1 inhibitors.
- **R**ash (I mean skin rash)
- **I**nduce bronchial asthma. ☺
- **N**ephrotoxicity : Interstitial nephritis and rarely acute renal failure.

Precautions :

- Never exceed therapeutic doses & Never combine more than one NSAID.
- Avoid long term use if possible.

2- **Cortisone** :

- Small dose of cortisone may be given (7.5 mg/d).
- Systemic steroids uncommonly needed nowadays.
- May be used in high dose in treatment of extra-articular manifestations.
- SE of cortisone : see Endocrinology book page 62

NB

Analgesics & cortisone improve pain but don't prevent joint damage or slow the disease progression.

3- Disease Modifying Anti-Rheumatic Drugs (DMARDs) :

- Group of drugs used in systemic rheumatic disease aiming for minimizing disease activity & progression.
- These drugs are slow acting drugs (their effect takes 4-8 weeks to appear).
- Should be used as early as possible to induce remission & avoid erosive changes.
- Mechanism of action : exact mechanism is unknown
 - a. Inhibition of lysosomal enzymes, phagocytosis & prostaglandins.
 - b. Inhibitory effects on the immune system.
 - c. Some has antimicrobial activity (e.g. sulfasalazine)

i- Gold salts : (Na aurothiomalate)

- Dose : 50 mg/week **IM** for about 20 weeks (Total dose :1000 mg)
- SE : DHP ☺
 - **D**epression of bone marrow, **D**ermatitis.
 - **H**ypersensitivity.
 - **P**roteinuria.
- Precaution :
 - Stop if proteinuria > 2g /24h
 - Stop if WBCs < 3000 or platelets < 100000

ii- Penicillamine : ↓↓ RF

- Dose : 250 mg/d
- Response : within 4-6 months.
- SE : As Gold + SLE.

iii- Chloroquine :

- Dose : 250 mg/d
- Response : Within 4-6 months.
- SE : 👁 Retinopathy, Corneal opacity NOT Cataract , Skin rash. MCQ
- Precaution : Request fundus examination before use & every 6 months.

iv- **Immunosuppressive drugs** : see below.

v- **Sulfasalazine** :

- Mode of action : antifolate.
- Dose : 0.5 - 1 gm/d then increase to 2-3 gm/d over few weeks.
- Side effects : headache, skin rash, GIT irritation, leucopenia, reversible depression of sperm count.

vi- **Biologic agents** : see below

4- **Immunosuppressive** :

i- **Methotrexate** :

- Most popular DMARDS.
- **Dose** : 7.5mg/ week. (oral, SC, IM)
- **Side effects** :

- ☠ Anemia : folic acid deficiency **MCQ**
- ☠ **B**one marrow failure.
- ☠ **H**epatotoxicity.
- ☠ **P**ruritus.
- ☠ **P**hotosensitivity.
- ☠ **p**igmentations.
- ☠ **P**ulmonary fibrosis & interstitial **p**neumonia.

○ **Precautions** :

- ✓ Never exceed therapeutic doses.
- ✓ Regular monitoring to screen for serious complications e.g. CBC , Liver & renal function tests. Chest X-ray may be required as there is a small risk of pneumonitis with methotrexate.
- ✓ Caution should be used when NSAIDs and penicillin are administered with methotrexate. These drugs may enhance its toxicity.
- ✓ Avoid alcohol & sun exposure.
- ✓ Since methotrexate reduces immune function, precaution should be taken to avoid all kinds of infection.
- ✓ Mouth sores may be reduced by folate supplementation.

ii- **Leflunomide** : (Avara).

- A new effective drug with rather rapid onset of action.
- Dose: 100mg/d for 3 days then maintenance 20mg/d.
- S/E : diarrhea, skin rash, hepatotoxicity & rarely bone marrow failure.

iii. **Azathioprine** :

- Dose : start with 1mg/kg/d then increase to reach 2-2.5 mg/kg/d.
- S/E : nausea, leucopenia, hepatotoxicity. Prolonged use increases the risk of lymphoma.

BIOLOGIC DISEASE-MODIFYING AGENTS**Tumor necrosis factor α (TNF α) blockers** : Infliximab, Adalimumab

- These agents are used in severe active rheumatoid arthritis when standard disease- modifying therapy has failed (usually given in combination with methotrexate)
- These drugs block the action of cytokines (chemical mediators)
- The onset of action is rapid compared with traditional disease – modifying drugs (2 weeks).
- S/E : Expensive, Infections e.g. TB

Interleukin-1 blocker (anakinra)

- It blocks the biologic activity of IL-1 including inflammation & cartilage degradation associated with rheumatoid arthritis.

**(C) Intra articular injection of cortisone :****Indication:**

- Inflammation of tendon (e.g. tendon achillis).
- Used for joints that remain painful despite of general measures.

S/E: - Infection $\Rightarrow$ septic arthritis - Rebound pain.

(D) Surgical treatment:

- Synovectomy. - Arthrodesis. - Joint replacement.

VARIANTS OF RHEUMATOID ARTHRITIS**I. Sjögren's syndrome :**

- It is classified as primary when it occurs in the absence of another connective tissue disease, and as secondary when found in association with another connective tissue disease such as RA, SLE, MCTD.
- There is an association with HLA-B8, HLA-DR3
- Clinical picture :
 - ✧ Arthritis : usually non erosive polyarthritis.
 - ✧ Dry eye (xerophthalmia), dry mouth (xerostomia), dry skin & dry vagina.
 - ✧ Lymphadenopathy: there is increased incidence of lymphoma.
 - ✧ Renal tubular acidosis & Raynaud's phenomenon.
 - ✧ Associated autoimmune diseases : myasthenia gravis, autoimmune hepatitis, thyroid diseases.
- Investigations :
 - ✧ Highest incidence of **rheumatoid factor** is found in : Sjogren's syndrome. (90%) **MCQ**
 - ✧ Anti Ro, anti La antibodies. (*Anti Ro is of particular interest because it can cross the placenta and cause congenital heart block*).
 - ✧ +ve ANA
- Treatment :
 - ✧ Hydroxychloroquine, low dose cortisone or methotrexate.
 - ✧ Xerophthalmia : treated by artificial teardrops & corneal protection by soft contact lenses.
 - ✧ Xerostomia : may be managed by parasympathomimetic.
 - ✧ Dry vagina is treated with lubricants e.g. K-Y jelly.

II. Felty's syndrome :

- Arthritis (Like RA).
- Splenomegaly with hypersplenism. (No hepatomegaly)
- Pancytopenia.
- Cortisone is a drug of choice.



III. Sero-negative arthropathy: (Sero -ve spondylopathy)**General features:** 8 features

- Rheumatoid factor: negative (*the reason for the name*).
- Central (spondylitis and / or sacroiliitis) > peripheral arthritis.
- Asymmetrical peripheral arthritis.
- HLA-B27 (EXCEPT in Behcet's syndrome) MCQ
- +ve family history.
- Red eye.
- Erythema.
- Enthesitis (inflammation at sites of tendon insertion).

1- Reactive arthritis :

- It is a sterile arthritis which occurs following an infection.
- Causative organisms :
 - ✂ Chlamydia trachomatis : urogenital infection.
 - ✂ Salmonella, Shigella, Yersinia : GIT infection (bacillary dysentery)
- Reactive arthritis may be just arthritis, but sometimes the clinical triad of Reiter's disease may occur.

Reiter's syndrome : ♂ > ♀ (10 : 1)It is a form of reactive arthritis characterized by a Clinical triad of : 🎵 🎵

1. Arthritis : Asymmetrical, oligoarticular, usually involves big joints of LL (knee, ankles, feet). Sacroiliitis & spondylitis may occur.
2. Conjunctivitis (red eye). Can't see, can't pee, can't climb the tree
3. Urethritis, cystitis.

Treatment :

- i. Non pharmacological : The same as RA
- ii. Pharmacological :
 - Antibiotics for infections.
 - NSAIDs for arthritis.
 - Recurrent or chronic symptoms may need DMARDs.

2- Behcet disease: BD

- It is a **systemic vasculitis** of unknown etiology which can involve large, medium and small arteries and veins.
- There is an association with **HLA-B5**
- **Clinical picture** : highly variable with recurrence and remissions

➤ **Diagnostic criteria :**

Recurrent painful oral ulcer (100%) : Initial criteria for diagnosis require the occurrence of at least 3 episodes of painful **oral aphthous ulcers/year**. To confirm the diagnosis, at least two of the following must also be demonstrated :

- i. Recurrent painful genital ulcers that heal with scarring. (80%)
- ii. Recurrent anterior uveitis or retinal vasculitis (60%) : may lead to blindness.
- iii. Skin lesions (60%) : including erythema nodosum or acneiform lesions.
- iv. Positive pathergy skin test : defined as the formation of a sterile erythematous papule 2 mm in diameter or larger that appears 48 hours following a skin prick with a sharp sterile needle.

➤ **Other features :**

- Arthritis : non-erosive, asymmetrical oligoarthropathy, involves big joints.
- Vasculopathy :
 - Unlike most forms of vasculitis, both arteries and veins, of all sizes, are involved.
 - Venous thrombosis, Budd-chiari syndrome, IVC & SVC clot.
 - Aneurysms of pulmonary arteries may lead to massive lung hemorrhage
- GIT : Ulcerations may occur anywhere in the GIT. The terminal ileum and cecum are common sites. It may be difficult to distinguish from inflammatory bowel disease (such as Crohn's disease).
- CNS : aseptic meningitis, strokes, cerebellar ataxia, cranial nerve palsies, psychiatric disorders.
- Cardiac : coronary vasculitis, pericarditis.

- **Investigations** : Non specific, reflect inflammatory state ($\uparrow$ ESR, CRP)
- **Treatment** : symptomatic treatment
 - ✗ NSAIDs for arthritis and thrombophlebitis.
 - ✗ Systemic anticoagulant is often used in patients with thrombosis.
 - ✗ Mouth ulcers : oral washes, topical steroids.
 - ✗ Genital ulcers : topical steroids, colchicine.
 - ✗ Anterior uveitis : systemic steroids, colchicine, cyclosporine.
 - ✗ Anti-TNF therapy in severe cases.

3- Ankylosing spondylitis:

- It is a chronic systemic inflammatory disorder of the axial skeleton. The inflammatory process frequently results in gradual fibrous & bony ankylosis.
- 0.1 % of population.
- ♂ : ♀ = 3:1 ⊗
- Age : < 40 years (Onset after age of 40 is uncommon)
- Clinical picture : **7 A**
 - Arthritis : mainly Sacroiliac joints and the spines.
 - Back pain with prolonged morning stiffness. This stiffness improves with movement and exercise. The earliest most typical site is sacroiliac joints.
 - Sacroiliac joints tenderness & decreased spinal motility.
 - Sometimes reduced chest expansion due to costovertebral joint involvement.
 - Peripheral joints (30%).
 - Anterior uveitis. (25%).
 - Achilles enthesitis (tendinitis).
 - Aortic regurgate (10%).
 - Atlantoaxial subluxation.
 - Amyloidosis.
 - Apical pulmonary fibrosis.
 - Chronic prostatitis.

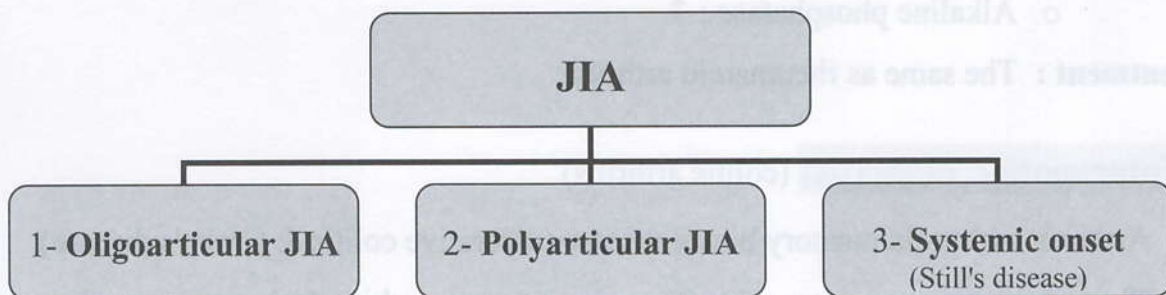
7. JUVENILE IDIOPATHIC ARTHRITIS (JIA)

previously termed " juvenile chronic arthritis (JCA), juvenile rheumatoid arthritis "

3 criteria must be met to diagnose JIA :

- Persistent arthritis of more than 3 months.
- Onset : under the age of 16.
- Exclusion of other diseases that may cause arthritis e.g. septic arthritis.

Classification : The 3 major types of JIA are :



1. **Oligoarticular (Pauciarticular)** : most common, 60% of JIA

- Affects 4 or fewer joints, usually not symmetrical.
- Usually involves the large joints > small joints.
- There are 2 types :
 - a) Early childhood onset : younger girls, usually ANA +ve, at risk for developing an anterior uveitis. So, routine eye exam every 3 months is recommended.
 - b) Late childhood onset : usually older boys with sacroiliitis & HLA-B27

2. **Polyarticular** : 30% of JIA

- Affects 5 or more joints.
- Symmetrical polyarthritis usually of small joints > large joints.
- This type of JIA is more common in girls than in boys.
- Children with polyarticular JIA are also at risk for developing chronic uveitis and should also be monitored by an ophthalmologist.

3. **Systemic onset JIA** : (Still disease)

- A disease of under-fives but adult cases may occur.
- Fever (*high with spikes up to 40°C daily*), skin rash, Splenomegaly.
- RF : usually -ve.
- Late arthropathy. **So**, misdiagnosed as hematological disorder.

	Oligoarticular	Polyarticular	Systemic (Still disease)
Frequency (%)	60	30	10
Number of joints	4 or less	5 or more	Variable
Female : Male ratio	5:1	3:1	1:1
Extra-articular	Rare	Moderate	Prominent
Uveitis (%)	20 ☠	5	Rare
Rheumatoid factor	Rare	15 %	Rare.
ANA	85 %	40 %	10 %
Prognosis	Good	Moderate	Moderate

I know not with what weapons World War III will be fought, but World War IV will be fought with sticks and stones.

Albert Einstein

SYSTEMIC LUPUS ERYTHEMATOSIS

(SLE)

Definition:

It's a systemic connective tissue disorder characterized by extra-articular & articular manifestations, most probably autoimmune.

Etiology:

Is still questionable , most probably autoimmune : defect in T suppressor lymphocyte
 → ↑↑ autoantibody → immune complexes which can involve tissue anywhere in the body → systemic manifestations.

- Genetic factor : +ve family history & HLA association (HLA DR2, HLA B8)
- Environmental factors : sun light, infections may play some role.
- Drugs (*drug induced lupus*): **hydralazine**, INH, penicillamine & phenytoin.
- Hormonal factor also may play an important role: e.g. estrogen, this explains why SLE is common in ♀ especially in child bearing period & exacerbation in pregnancy.

Pathology :

I- Articular :

Synovitis which is usually not erosive (no cartilage destruction).

II- Extra articular:

Deposition of immune complex in a variety of areas of the body: skin, kidney (glomeruli), heart, lung, CNS....

N.B: - when only skin is involved, this condition is called discoid lupus.

- When internal organs are involved, this condition is called SLE.

Clinical picture :

More common in ♀ (20 - 45y')

♀ : ♂ (10 : 1) ☺

I- General : fever, fatigue, sweating.

II- Extra articular manifestations:

i- **Skin** : 6

↳ Malar rash : erythema over the cheeks.

↳ Butterfly rash : erythema on the cheeks & nose

↳ Discoid rash : mnemonic, ESPT

Erythema, Scar formation, skin Pigmentation & Telangiectasia occur over the face & neck.

↳ Photosensitivity :

Skin rash as a result of unusual reaction to sunlight.

↳ Alopecia.

↳ Vasculitis :

- Purpura, leg ulcer

- Raynaud's phenomenon: poor circulation to the fingers & toes with cold exposure.



ii- **Renal** : (Lupus nephritis)

Details : see nephrology book

- Renal disease is common.
- Note that drug induced lupus rarely affects the kidneys.
- Patients with lupus nephritis generally have abnormalities on urinalysis: Proteinuria, either asymptomatic up to nephrotic range. Hematuria and casts may be seen.
- Acute or chronic renal failure may develop.
- Needless to say that patients may suffer from other symptoms of lupus unrelated to kidney function e.g. arthralgia, fever, fatigue, psychosis,
- Renal biopsy should be considered in any patient with SLE who has clinical or laboratory evidence of active nephritis.

• **WHO CLASSIFICATION OF LUPUS NEPHRITIS :**

Class I : Normal glomeruli	○ Mild proteinuria.
Class II : Mesangial affection	○ Asymptomatic proteinuria or hematuria. ○ This form typically responds completely to treatment with corticosteroids.
Class III : Focal proliferative GN	○ Often responds to treatment with high dose corticosteroids.
Class IV : Diffuse proliferative GN	○ This form is mainly treated with corticosteroids & immunosuppressive drugs.
Class V : Membranous GN	○ Characterized by extreme edema and protein loss (nephrotic syndrome)
Class VI : Sclerosing GN	○ Significant renal insufficiency or end stage renal disease in most cases. ○ Unlikely to respond to medical therapy.

iii- **Cardiac:**

- ↳ Pericarditis.
- ↳ Myocarditis → HF.
- ↳ **Libman endocarditis** (non-infective endocarditis) → Aortic & mitral regurge.
- ↳ Systemic Hypertension.
- ↳ Ischemic heart disease (accelerated athrosclerosis).

iv- **Chest:**

- ↳ Pleurisy & pleural effusion.
- ↳ Interstitial pulmonary fibrosis.
- ↳ Pulmonary infarction (shrinking lung syndrome)
- ↳ Pulmonary hypertension.
- ↳ **ARDS**

V- **CNS:**

- ↳ Headache.
- ↳ Depression
- ↳ Neuropathy
- ↳ Myopathy
- ↳ Chorea
- ↳ Epilepsy
- ↳ Cerebral vasculitis (lupus cerebritis) → stroke.

- Nervous manifestations may be due to diffuse cerbritis, vasculopathy, thrombosis, infection or drug effects.

vi- **Eye:**

- ↳ Conjunctivitis.
- ↳ Scleritis.
- ↳ Anterior uveitis
- ↳ Retinal vasculitis.

vii- **GIT:**

- ↳ Nausea & vomiting.
- ↳ Painless oral ulcer.
- ↳ Esophagitis.
- ↳ Gastritis & peptic ulcer.
- ↳ Vasculitis : Abdominal Pain.
- ↳ Pancreatitis.
- ↳ HSM.

Viii- **Blood:**

- ↳ ↓ RBCs : Anemia of chronic disease, hemolytic anemia.
- ↳ ↓ Platelets & WBCs : may be due to the disease or a side effect of pharmacological treatment.
- ↳ Antiphospholipid antibody syndrome ⇔ thrombo-embolism.
- ↳ Lymphadenopathy & Splenomegaly are frequently seen.

III- Articular manifestations: 3D**i- Distribution :**

- 1- Polyarthropathy.
- 2- Symmetrical.
- 3- Affects mainly the peripheral joints e.g. UL, LL
- 4- Affects mainly small Joints e.g.: Hands, feet.
- 5- Usually Not erosive: (No deformity).

ii- Description : 🎵🎵

- *Arthralgia* more than arthritis (pain only).
- *Myalgia* is common.

iii- Deformity :

- Rare, may occur due to tendon or ligament laxity.
- Necrosis of hip due to steroid therapy.

Pregnancy & SLE:

- 1- Fertility is unaffected. (normal & safe pregnancy & she is often able to deliver normal infants).
- 2- Disease exacerbations during pregnancy may occur.
- 3- Preeclampsia & abortion occur more frequently in pregnant patient with lupus.
- 4- Child born to mother with SLE: skin manifestations & congenital heart diseases.

Cause of death in patients with SLE:

- Nephritis
- Infection
- SLE → ↑ risk for developing cancer (blood, breast).
- Coronary diseases.
- Stroke
- MI

N.B. Ten years survival > 90%

Investigations:**(1) Blood picture:**

- ✧ Anemia : anemia of chronic disease, hemolytic anemia.
- ✧ Leukopenia ($<4000/\text{mm}^3$)
- ✧ Thrombocytopenia ($<100000/\text{mm}^3$)
- ✧ Lymphopenia.
- ✧ ESR : $\uparrow\uparrow$
- ✧ CRP: normal but $\uparrow$ only with infection.
- ✧ $\downarrow$ C_3 & C_4 : Consumed.

In one word**Investigations of SLE :**

Scheme +

- Lymphopenia
- C_3 & C_4 : $\downarrow$
- Renal function tests.

(2) Serological tests :**➤ Non specific Ab:**

- LE cells: +ve in 80% of cases.
- Rheumatoid factor (RF): +ve in 25 %
- Anti-nuclear Ab (ANA): +ve in 95-100% (*most sensitive*). Positive ANA not diagnostic, but negative test argues strongly against SLE.

Causes of +ve ANA: (+ve in 5% of normal population)

- SLE (95%)
- Rh. Arthritis (30%).
- Scleroderma (90%).
- Sjögren's syndrome (60%).
- 1ry biliary cirrhosis.
- Infective endocarditis.
- Old age.

➤ Specific antibodies :

- Anti double stranded DNA (dsDNA): in high titre is very specific to SLE.
- Anti smith (Anti-SM): indicates poor prognosis.
- Anti Ro (SS-A), Anti La (SS-B) : found in ANA -ve lupus.
- **Anti histone : specific to drug induced lupus.**
- **Anticardiolipin Ab** : Antiphospholipid antibody syndrome.

MCQ**(3)- X ray : Osteoporosis.**

Chest X-ray: pleural effusion.

(4)- Aspiration of synovial fluid : Ab**(5)- Investigations for lupus nephritis : urine analysis & renal function tests.**

The eleven criteria used for diagnosing SLE: (American College of rheumatology).

- 1- Malar or butterfly rash.
- 2- Discoid rash.
- 3- **P**hotosensitivity.
- 4- **P**ainless oral ulcer.
- 5- **P**eripheral joints arthritis : 2 or more peripheral joints.
- 6- **P**leurisy or pericarditis.
- 7- **P**roteinuria.
- 8- **P**sychosis or seizures.
- 9- **P**ancytopenia.
- 10- +ve ANA antibody.
- 11- +ve anti ds DNA ab or anti-sm ab.

2 Rash, 2 Ab & 7 Ps

The diagnosis of SLE is strongly suggested, when a person has 4 or more of these criteria.

2012 SLICC criteria for SLE

- *SLICC : Systemic Lupus International Collaborating Clinics*
- Classify a patient as having SLE if :

A. The patient has biopsy-proven lupus nephritis and with ANA or anti-dsDNA antibodies.

OR

B. The patient satisfies four criteria including at least one clinical and one immunologic criterion.

Clinical criteria :

1- Acute or subacute cutaneous lupus	Acute (Malar rash or photosensitivity), subacute cutaneous lupus (annular or psoriaform patch).
2- Chronic cutaneous lupus	Discoid rash
3- Oral ulcers	Palate, buccal, tongue or nasal ulcers in the absence of other causes, such as Behçet.
4- Nonscarring alopecia	Diffuse thinning or hair fragility with visible broken hairs in the absence of other causes such as alopecia areata, drugs, iron deficiency and androgenic alopecia.
5- Synovitis	Involving two or more joints
6- Serositis	– Pleurisy for more than 1 day or pleural effusions or pleural rub. – Pericarditis, pericardial effusion or pericardial rub <i>in the absence of other causes, such as infection, uremia.</i>
7- Renal	Proteinuria > 500 mg /d or red blood cell casts.
8- Neurologic	Seizures, psychosis, mononeuritis multiplex, myelitis, peripheral or cranial neuropathy.
9- Hemolytic anemia	
10- Leukopenia (<4000/mm ³) OR Lymphopenia (<1000/mm ³)	At least once in the absence of other known causes such as Felty's, drugs ..
11- Thrombocytopenia (<100,000/mm ³)	At least once in the absence of other known causes such as drugs, TTP.

Immunologic criteria :

- | |
|---|
| 1. ANA |
| 2. Anti-dsDNA |
| 3. Anti- SM |
| 4. Antiphospholipid antibody : Lupus anticoagulant, high titer anticardiolipin. |
| 5. Low complement : Low C3, low C4 |
| 6. Direct Coombs test : In the absence of hemolytic anemia |

Treatment of SLE:

7

- There is no cure for SLE.(SLE is considered incurable, but highly treatable)
- Goal of treatment is to relieve symptoms by decreasing inflammation, ↓↓ autoimmune activity.
- Depends on severity and organ involvement.

1- General prophylactic measures:

- a. Rest.
- b. Sensitivity to light is treated by → protective clothing, sunglasses & sunscreens.
- c. Avoid drug inducing SLE.
- d. Psychological treatment.

2- NSAIDs: are used to treat arthritis & pleurisy.

3- Cortisone: for extra-articular manifestations.

- Topical : cortisone cream for skin rash.
- Systemic :

Pulse dose: 1000mg/d IV for 3 days, followed by 60mg/d till activity of the disease disappears (↓↓ symptoms & signs , -ve Anti DNA).

Then followed by **maintenance dose** : 10:15mg/d

S/E of cortisone : see Endocrinology book.

4- Hydroxychlorquine : Is sometimes used with cortisone (low dose) for skin manifestations & arthritis resistant to NSAIDs.

5- Immunosuppressive drugs : for severe cases resistant to cortisone therapy

- (MAC):
- Methotrexate.
 - Azathioprine.
 - Cyclophosphamide.

6- Plasmapheresis : in SLE patients with serious brain or kidney manifestations.

7- Treatment of complications:

- Removal of spleen is sometimes done for thrombocytopenia.
- End stage kidney damage : dialysis or kidney transplant.

Women tend to love men in their presence, while men tend to love women in their absence

Variants of lupus :

MCQ

(1) DRUG INDUCED LUPUS (DIL)

- More common in ♂
- History of drug intake : Hydralazine INH, Phenyton, Penicillamine, Procainamide, α methyl dopa.
- There is NO contraindication to using these drugs in idiopathic SLE.
- **Renal, CNS, skin features of SLE are rare in DIL.**
- Pathogenesis : Unknown.
- Investigations: Anti-histone antibody, ANA are +ve, but Anti-DNA Abs are absent.
- Treatment : withdrawal of the drug & short course steroid are all that we need.

(2) ANTIPHOSPHOLIPID SYNDROME**Definition :**

Recurrent attacks of venous or arterial thrombosis and thrombocytopenia in association with laboratory finding of antibodies against phospholipids.

Classification :

- Primary : occurs in patients without clinical evidence of another autoimmune disease.
- Secondary : occurs in association with autoimmune disease e.g. lupus.

C/P :**a) Vascular thrombosis :**

- Cerebral infarction, less common, coronary, retinal & visceral.
- Venous thrombosis : especially deep venous thrombosis.

b) Obstetric : Recurrent abortions, more common in the 2nd or 3rd trimester.**c) Cardiac : Valvular insufficiency, Libman endocarditis.****d) Non-thrombotic neurologic symptoms : Migraine, chorea, seizures, Guillian-Barre syndrome or dementia.**

Mechanisms of thrombosis in antiphospholipid syndrome :

1. Antiphospholipid antibodies interfere with the function of phospholipid-binding proteins involved in the regulation of coagulation.
2. Activation of endothelial cells.

Investigations :**I. Laboratory :**

- a) CBC : anemia, thrombocytopenia.
- b) Serologic tests :
 - **Anti-cardiolipin antibodies** (IgG, IgM)
 - Anti- β_2 glycoprotein I antibodies (IgG, IgM)

II. Imaging studies : for confirming a thrombotic event

- CT, MRI of the brain (cerebral stroke), chest (pulmonary embolism), abdomen (Budd-Chiari syndrome).
- Doppler ultrasound : for possible detection of DVT.
- Two dimensional echocardiography : for possible detection of endocarditis, valvular insufficiency.

Treatment :**✎ Treatment of thrombosis :**

- IV or SC heparin followed by warfarin therapy.
- During pregnancy : patients with a history of thrombosis receive therapeutic doses heparin during pregnancy, long term anticoagulation is then continued postpartum.

✎ IV steroids.**✎ Cyclophosphamide.****✎ Plasmapheresis.**

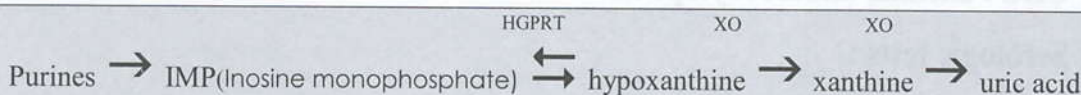
GOUT

Definition:

Gout is a disease which is characterized by tissue deposition of monosodium urate crystals due to hyperuricemia that results in :

- *Gouty arthritis.*
- *Tophi.*
- *Gouty Nephropathy.*

- Gout is the most common type of inflammatory monoarthritis.



Etiology:

- ↑ Production of uric acid (Metabolic gout).
- ↓ Excretion of uric acid (Renal Gout).

(A) : ↑ Production:

- 1ry : Enzyme defect : ↓↓ HGPR (hypoxanthine -Guanine- phosphoribosyl - Transeferase).
- 2ry : leukemia, lymphoma, sarcoidosis, severe psoriasis.

(B) : ↓↓ Excretion:

- 1ry : Idiopathic (Isolated tubular defect).
- 2ry :
 - Renal Failure.
 - Acidosis e.g. increased lactic acid production from alcohol, starvation.
 - Hyperparathyroidism, Hypothyroidism.
 - Dehydration → ↓ Renal Flow.
 - Drugs: e.g. Diuretics, Pyrazinamide, Low dose aspirin.

N.B. Causes of hypourcemia :

- Pregnancy → GFR ↑↑
- Fanconi syndrome.
- Iatrogenic : Allopurinol.

Pathology:

Acute gouty arthritis :

Uric acid in itself is not irritant to joint & urate crystals can be found in asymptomatic joints. but when urate crystals phagocytosed by macrophage → release of lysosomal enzymes which produce inflammatory reaction → acute gouty arthritis.

Chronic gout :

Deposition of uric acid in:

- **Joint:** chronic erosive arthropathy.
- **Kidney:** gouty nephropathy.
- **Tissue:** Tophi.

Clinical picture: ♂ > ♀ ☹ 40-50 y'

Asymptomatic hyperuricemia :

- Just elevated levels of uric acid.
- 90% of hyperuricemic patients never develop gout.

Symptomatic:**1- Acute gouty arthritis: 3D****Precipitating factors :**

- Excess protein, Alcohol.
- Drugs e.g. thiazide, lasix.
- Surgery, Trauma.
- Infection.
- Dehydration.

Distribution :

- Monoarthritis.
- Usually in the first metatarsophalangeal joint (of the *big toe*).
- Other sites : the ankle, the dorsum of the foot, the knee & occasionally the joints of upper extremity.
- **Not erosive.**



Description :

- Hotness, Redness, Tenderness, Swollen & limitation of movement.
- Acute attack is severely painful, it often develops overnight and reaches a peak within hours (waking the patient in the early morning)
- Dramatic relief of pain with colchicines is suggestive.
- Slight fever & chills may be present.

Deformity : No.

DD of acute gouty arthritis : It should be differentiated from other causes of monoarthritis e.g. septic arthritis see later

2- Chronic gout :**i- Arthritis :**

- Polyarthritis.
- Asymmetrical.
- Erosive.
- Remission & exacerbation.
- Deformity : yes.

ii- Gouty nephropathy:

- precipitation of uric acid into renal tubules → ARF.
- Precipitation of uric acid in renal interstitium → chronic Interstitial nephropathy → CRF.
- Precipitation of uric acid in urinary tract → urate stones (Hematuria , infection).

iii- Tophi:

- Occurs with severe hyperuricemia.
- Tophi deposits occur usually in the skin around the joints, extensor surface of fingers & ear lobule.
- May ulcerate & discharge chalky paste material.

Investigations:

i- Uric acid (N= 2.5 - 7mg%) : > 7 mg% in ♂ , > 6 mg% in ♀

NB

- It is a biochemical hallmark of gout, but not by itself diagnostic for gout.
- Minority of patients showing acute gout with normal serum uric acid, so normal serum uric acid does not exclude the diagnosis of gout.

ii- X ray :

- Soft tissue swelling around the affected joints.
- punched out lesion & deformity in chronic gout.

iii- Aspiration of synovial fluid (Arthrocentesis) :

- Urate crystals by Polarized microscopy.
- It is the single most useful diagnostic study in initial evaluation of monoarthritis.

iv- Biopsy from tophi.

v- Blood picture : leucocytosis, $\uparrow$ ESR, $\uparrow$ CRP.

vi- U/S kidney.

Treatment:**i- Asymptomatic hyperuricemia:**

No need for treatment except with :

- +ve family history.
- Uric acid > 11 mg%
- $\uparrow\uparrow$ excretion of uric acid in urine.

ii- Acute gouty arthritis:

- **NSAIDs:**

- Indomethacin : 75mg & then 50mg/6h for 2 or 3 days.
- Diclofenac : 75 mg & then 50mg/6h
- Don't use aspirin because it can alter uric acid level.

- **Cholchicine :**
 - 1.2 mg at the first dose followed by 0.6 mg one hour later.
 - S/E: diarrhea, vomiting. Contraindicated in renal failure.
- **Short term cortisone.**

III- Chronic gout : (hypouricemic drugs).

1- Diet :

- Avoid excessive meat, fish & poultry intake.
- Avoid alcohol .
- Excessive fluid intake (2 – 3 L daily)
- Try other good protein such as eggs.

2- Medical treatment :

- **Allopurinol** (zyloric) :
 - Dose : 100-300 mg/d
 - Mech. : xanthine oxidase inhibitor.
 - S/E : fever, diarrhea, Allergy , BM depression.
 - Allopurinol is NOT used during the acute gouty arthritis as it may aggravate the attack. **MCQ**
- **Febuxostat** : is a new xanthine oxidase inhibitor. Dose: 40 mg/d. S/E : nausea, diarrhea, rash, arthralgia, headache, increased hepatic serum enzyme.
- **Uricosuric drugs (probenecid)** :
 - Dose : 0.5-1gm/12h.
 - Used with alkalinization of urine.
- **Pegloticase** :
 - It is a new drug for the treatment of severe, treatment-refractory, chronic gout.
 - Pegloticase is a recombinant porcine-like uricase. It metabolises uric acid to allantoin. This reduces the risk of precipitates, since allantoin is five to ten times more soluble than uric acid.
 - Pegloticase is given as an intravenous infusion every two weeks.

3- Joint aspiration & intraarticular injection of cortisone.

4- Prevention of nephrolithiasis :

- Urine alkalinization : by the use of sodium or potassium citrate or acetazolamide, 500 mg at bedtime.
- Excessive fluid intake (2 – 3 L daily)

Pseudogout (chondrocalcinosis)**Definition:**

- Deposition of Ca pyrophosphate (CPP) crystals in cartilage.
- Can cause monoarthritis clinically indistinguishable from gout – Pseudogout

Etiology:

- Idiopathic.
- It can occur with certain metabolic diseases: hypercalcemia, DM, CRF, hemochromatosis.

Clinical picture: ♂ = ♀

- **Mono** arthritis especially in the knee.
- May be asymptomatic (deposition of CPP in cartilage).

Investigations:

- X ray: cartilage calcification.
- Ca-pyrophosphate crystals in synovial fluid.
- ESR ↑

Treatment: NSAID - Intra-articular cortisone**Pseudo-Pseudo Gout**

- Hydroxy appatite arthropathy.
- ♀ > ♂
- Shoulder joint is the commonest site.

VASCULITIS**Definition :**

Vasculitis is a group of clinical syndromes characterized by inflammation that predominately involves the blood vessels of unknown etiology.

Etiology : As scheme.**Classification :** (according to the size of vessel involved)

- Small vessels :
 - ♪ Henoch-Schönlein purpura .
 - ♪ Wegener's granulomatosis .
 - ♪ Vasculitis of RA , SLE .
- Medium sized vessels :
 - ♪ Polyarteritis nodosa .
 - ♪ Kawasaki's disease .
 - ♪ Churg-Strauss syndrome .
- Large vessels :
 - ♪ Takayasu's disease .
 - ♪ Giant cell arteritis (temporal arteritis) .
 - ♪ Aortitis associated with ankylosing spondylitis .

Clinical picture :

General : - Fever - Fatigue - Sweating -Anorexia & loss of weight.

Articular manifestations : Arthralgia, arthritis (usually oligoarthropathy), myalgia.

Extra-articular manifestations : The same as general scheme

But, each type of vasculitis can also cause **specific** manifestations depending on which vessels & which organs are affected.

How to reach diagnosis of a case of vasculitis :

- 1) Exclude other conditions that simulate vasculitis :
 - Atherosclerosis.
 - Vascular spasm : e.g. iatrogenic (ergots, cocaine)
 - Embolic conditions : Infective endocarditis, myxoma.
 - Conditions with increased thrombotic tendency : DIC, TTP, antiphospholipid syndrome.
- 2) Exclude conditions which can cause 2^{ry} vasculitis :
 - Connective tissue diseases e.g. RA, SLE.
 - Malignancy : lymphoma, leukemia.
 - Drugs : NSAIDs, antibiotics.
 - Infections : rheumatic fever, infective endocarditis, Lyme's disease.
 - Cryoglobulinemia.
- 3) Take notice of the patient's age & gender.
- 4) Decide the extent of organ involvement and try to fit the finding into a specific vasculitic syndrome.

Investigations :

- 1) Laboratory :
 - CBC, ESR, CRP, urinalysis, renal function tests, hepatic enzymes.
 - Rheumatoid factor, ANA, Antiphospholipid antibodies.
 - Anti-neutrophil cytoplasmic antibodies (ANCA) : +ve in WG , -ve in PAN
- 2) Vascular imaging : Duplex, Angiography.
- 3) Other imaging studies :
 - X-ray and CT scan for chest.
 - Echocardiography.
 - Abdominal US or CT.
- 4) Biopsies : May be needed for confirmation or exclusion e.g. skin, muscle, renal, temporal arteryetc

Henoch-Schönlein purpura

(Anaphylactoid purpura , Allergic purpura)

Definition :

- It is a type of small vessel vasculitis which occurs mainly in children.
- It is the most common cause of non thrombocytopenic purpura in children.
- Age peak : 2- 8 years.

Clinical picture :

1) Skin : 100%

Palpable Purpuric rash especially over buttocks & extensor surface of legs.

2) Joints : 75%

- o Migratory polyarthritis.
- o Particularly knees and ankles.

3) Abdominal pain & GIT bleeding due to mesenteric vasculitis. ?

4) Renal involvement : (*the worst prognosis*)

- o Focal glomerulonephritis.
- o Asymptomatic proteinuria & hematuria.

Investigations :

- 1) All investigations of bleeding tendency are normal except Hiss test may be +ve
- 2) Platelet count and function are normal.
- 3) Elevated serum IgA level is suggestive.
- 4) Skin biopsy : IgA deposits.

Treatment & prognosis :

- Spontaneous resolution within a month is commonest outcome in children.
- Chronic renal failure in 10% of cases.
- Steroids may improve the joints & gastrointestinal manifestations.

Wegener's granulomatosis

- Upper respiratory tract : Sinusitis , epistaxis.
- Lung : Pulmonary nodule.
- Kidney : Glomerulonephritis.
- Eye : scleritis.
- Ear : otitis media.
- cANCA : +ve in 90% of cases .
- Treatment is with high-dose steroids, methotrexate, and cyclophosphamide.

GIT involvement is uncommon

Churg-Strauss syndrome

- Bronchial asthma.
- Eosinophilia.

Kawasaki disease

- Usually in children.
- **Red eye** - **Red lips & mouth** - **Red hands & feet** - **Red skin (rash)**
- Cervical lymphadenopathy
- Vasculitis of coronary arteries : coronary aneurysm , myocardial infarction may occur.
- Treatment :
 - Aspirin & immunoglobulin are used.
 - **Cortisone is contraindicated** (↑ coronary aneurysms).

Takayasu's disease (*Pulseless disease*)

- Affects the aorta & its main branches e.g. subclavian artery producing :
 - Arm claudication .
 - Absent pulse .

Giant cell (temporal) arteritis (GCA)

- Vasculitis of large vessels affecting the cranial vessels especially branches of temporal & ophthalmic arteries.

Clinical picture : It usually affects the elderly (rare <50y) with female to male ratio 4 : 1

- General : malaise, anorexia, fever, night sweats, weight loss, depression.
- Unilateral throbbing headache, facial pain, scalp tenderness (*on brushing hair*).
- Visual disturbance up to sudden loss of vision. ☹
- Jaw claudication : due to ischemia of the masseters.
- Polymyalgia rheumatica : in 50% of cases
Syndrome of Proximal symmetrical muscle pain and stiffness worse after rest.

Investigations :

1. ESR : ↑
2. Temporal artery biopsy :
 - Necrosis of media with inflammatory cells e.g. lymphocytes & plasma cells.
 - Biopsy may be -ve, even in true cases, due to skip lesions. Don't withhold treatment whilst waiting for biopsy.

Treatment :

- ✎ Prednisolone 60 mg/d, immediately to prevent visual loss from ischemic optic neuropathy. Once blindness has occurred, steroid therapy of no value other than preventing blindness in the other eye.

Prognosis :

Most patients require >2 years of treatment. Relapse is common after stopping treatment (50% if stopped after 2 years).

Polyarteritis Nodosa**Definition :**

- Systemic necrotizing vasculitis with aneurysms formation, affecting medium sized arteries.
- If only small vessels are affected, it is called microscopic polyangiitis.

Etiology : Autoimmune, Hepatitis B play a big role (HBsAg +ve in 30% of cases)

Clinical picture: ♂ : ♀ = 2 : 1 ☹

- Renal (60%) :
 - Infarction rather than glomerulonephritis .
 - Hypertension & renal failure .
- Neurological :
 - Stroke .
 - Mononeuropathy , mononeuritis multiplex .
- **No** pulmonary involvement in classic PAN .
- Cardiac : coronary heart disease.
- GIT : mesenteric occlusion → acute abdomen.
- Genitourinary : Orchitis .
- Musculoskeletal : Arthralgia, myalgia.
- Hepatitis B is associated in 30% of cases.

Notice that it is Polyarteritis **NO**dosa : So, there are 2 **NO** : ☺

- ☞ **No** pulmonary manifestations.
- ☞ **No** cANCA.

Investigations :

- Biopsy .
- Angiography : shows multiple aneurysms .
- ↑ ESR , mild eosinophilia .
- HBsAg is +ve in 30% of cases .
- cANCA is -ve (+ve only in < 10% of cases) .

Treatment : Cortisone & immunosuppressive .

SYSTEMIC SCLEROSIS

"Scleroderma"

Definition :

- It's a connective tissue disorder characterized by thickening & fibrosis of the **skin** with involvement of blood vessels & internal organs.
- *In fact ,scleroderma literally means hard skin.*

Pathology :

- Collagen deposition all over the body.
- Vasculitis.

Clinical picture:

♀ : ♂ = 3 : 1 ☺

• Skin :

- Early : edema .
- Later : Induration (hardening) of the skin with loss of its elasticity.
- Skin hyper/hypo-pigmentation , ulceration & calcification .
- **Raynaud's phenomenon** : initial complaint in 70% , all patients eventually develop it during the course of their disease.

• GIT :

- Esophagus : **Dysphagia** , reflux . (80% of cases)
- Small intestine : Malabsorption syndrome .
- Large intestine : Constipation.

• Renal :

- Vasculitis of renal blood vessels : hypertension & CRF .
- **Scleroderma renal crisis** : it's a life-threatening condition manifested by sudden onset of malignant hypertension & ARF.

• Cardiac:

- Cardiomyopathy.
- Pericarditis & pericardial effusion.
- Ischemic heart diseases.
- Heart block : fibrosis of the conducting pathways.

- **Chest :**

- Interstitial pulmonary fibrosis .
- Pulmonary hypertension .
- Aspiration pneumonia : due to esophageal reflux .

- **CNS :** Headache and stroke during hypertensive renal crisis.

- **Musculoskeletal :**

- Arthralgia & rarely arthritis .
- Myopathy.

Variants (types) of scleroderma :



1- Diffuse scleroderma :

- Diffuse skin hardening involving trunk & proximal limbs as well as face & distal limbs .
- Severe internal organs damage and is generally more life threatening.

2- Limited scleroderma : (CREST syndrome)

- Skin hardening is limited to the fingers , face ,feet .
- Internal organ involvement is not severe, much better prognosis.
- CREST(Calcinosis, Raynaud's, Esophageal dysmotility, Sclerodactyly, Telangiectasia)

3- Localized scleroderma : (Scleroderma without internal organ involvement)

- Morphoea : local patches of scleroderma .

4- Systemic sclerosis sine (without) scleroderma : rare

- Internal organ involvement without skin manifestations .

5- Overlap syndrome : Scleroderma associated with other autoimmune disease.

Overlap syndrome (mixed connective tissue disease) :

This syndrome involves mixed features of at least 2 connective tissue disorders(SLE, Scleroderma, Polymyositis)

Investigations :

- ↑ ESR & CRP.
- ANA : +ve in 90% of patients.
- RF : +ve in 25 % of patients.
- **Anti Scl-70** : 30% of diffuse scleroderma .
- **Anti-centromere**: 70% of limited scleroderma (CREST syndrome)
- Biopsy.

Because not all people with scleroderma have these antibodies and because not all people with the antibodies have scleroderma, lab test results alone cannot confirm the diagnosis.

Treatment : " relieving symptoms and limiting damage."

- **Penicillamine** : slow progression of skin disease.(↓ collagen production)
- **Steroids** : indicated for treatment of inflammatory myositis,pericarditis or pulmonary fibrosis. **Steroids don't help the skin.**
- **Symptomatic treatment** :
 - Arthritis : NSAIDs.
 - Raynaud's : Ca channel blocker.
 - Renal crisis : ACE inhibitor is drug of choice "life saving".

Smile and the whole world will smile with you

‘Coz you smile when you feel good and you feel good When you smile’ ☺

OSTEOARTHRITIS

Definition :

- It's a degenerative arthritis ,characterized by breakdown of the cartilage with osteophytes formations, results from wear & tear on the joints.
- OA is the most common joint disease. MCQ
- OA unlike RA, is not an inflammatory disease.

Classification :

1- Primary : unknown etiology , genetic factors play a role.

2- Secondary : to

- Congenital : hip dislocation.
- Mechanical : occupational, sports injuries.
- Endocrinal : A cromegaly, m yxedema, hyperparathyroidism, DM
- Metabolic : hemochromatosis.
- Others : end of any inflammatory or infectious disease.

Risk factors :

- Aging (>45 y) : over time,as a joint moves, cartilage deteriorates & smooth surface becomes rough
- People with family history of osteoarthritis .
- Sex : more common in ♀ .
- Obesity : loading stress on weight bearing joints e.g. knee .
- Overuse of joints.

Common joints involved are :

MCQ

- Knees : the most common.
- Thumb base (1st carpometacarpal joint) : the 2nd most common
- Hips .
- Spine (cervical , lumbar)
- Distal interphalangeal joints (DIP) : Heberden's nodes.

- Proximal interphalangeal joints (**PIP**) : **B**ouchard's nodes.
- 1st metatarsophalangeal joint.

- ⇒ These joints are affected in asymmetrical oligoarticular or monoarticular pattern.
- ⇒ Metacarpophalangeal joints are uninvolved in primary OA.

Clinical picture : again, OA is the most common joint disease .

- 1- **Pain** (↑ by exercise & ↓ by rest) , stiffness may occur.
- 2- Crepitus on movement .
- 3- Minimal deformity & wasting of muscles around the joint .
- 4- **No systemic manifestations.**

Morning stiffness is not usually a prominent feature of OA, & when present , lasting no more than a quarter of an hour.

Investigations : Diagnosis is made on clinical & X-ray finding.

- **Normal laboratory finding.** (RF, ANA are -ve, ESR, CRP are normal)
- **X-ray** : (70% of 70 years old)
 - Joint space narrowing .
 - Osteophytes .
 - Subchondrial sclerosis.

Remember if ESR is elevated some other process is complicating OA e.g. septic joint or it is not OA !!

Treatment :

- Physiotherapy .
- Analgesics e.g. paracetamol : short courses .
- Intra-articular injection of steroid .
- Surgery.

POLYMYOSITIS & DERMATOMYOSITIS

Polymyositis is an autoimmune inflammation of skeletal muscle. When associated with cutaneous lesions it is called dermatomyositis.

Clinical picture : (MOHEM)

- (M) Myositis :
 - Mainly proximal muscles, symmetrical.
 - Involvement of esophagus : dysphagia.
 - Involvement of respiratory muscle : respiratory failure.
- (O) Oedema.
- (H) Heliotrope discoloration of the eyelids
- (E) Erythema :
 - Gottron's sign : symmetric erythema over the extensor surfaces of metacarpophalangeal joints, elbows and knees.
 - Diffuse flat erythema over the upper trunk and shoulder, the forehead
- (M) Malignancy : this occurs particularly in males with age above 50 years.

Investigations :

- 1- Elevated muscle enzymes : CK , SGOT , LDH .
- 2- Abnormal EMG .
- 3- Muscle biopsy .
- 4- Myositis specific antibody : Anti-Jo-1 (30%)

Treatment :

- ✎ Prednisone : 1mg/kg/d then kept at 10-15 mg/d.
- ✎ Immunosuppressive :
 - Methotrexate 5-20mg/week
 - Azathioprine 50-150 mg/d
 - Cyclophosphamide.
- ✎ IV gamma globulins and anti Rituximab : in severe cases.

INFECTIOUS ARTHRITIS

Classification :

- Bacterial septic arthritis :

a) Non gonococcal :

- Staph aureus.
- Streptococci .
- Gram-ve bacilli.

b) Gonococcal : caused by Neisseria gonorrhea.

- Lyme disease.
- Mycobacterial (immunocompromised)
- Fungal : (sporotrichosis most common)
- Viral arthritis.

Risk factors :

- Advanced age .
- Drug abuse .
- DM & suppressed immune system .
- Rheumatoid arthritis .
- Artificial joints, recent joint surgery or intra-articular injection of cortisone.

1- Bacterial septic arthritis :

a) Non-gonococcal septic arthritis :

Clinical picture :

- Flu-like symptoms : **Fever , Headache , Malaise , Anorexia .**
- Acute joint **pain**: usually single joint especially the knee. (80% of cases is monoarthritis)
- Signs of inflammation : hotness , redness , tenderness , swelling , limitation of movement .

Investigations :

- **Blood** : Leukocytosis , ↑ ESR , blood culture.
- **X-ray** : articular erosions may occur.
- **Synovial fluid examination** : +ve culture , ↑ neutrophils.

The synovial fluid should be examined for crystals, because gout & pseudogout can resemble septic arthritis clinically.

Treatment :

- **Antibiotic (IV)** : according culture & sensitivity test.e.g. : Ox, Clox, Diclox-acillin or vancomycin for staph. For about 4 weeks.
- Analgesics.
- Drainage of the infected joint daily.

b) Gonococcal arthritis :

- Most common in young healthy adults (females > males)
- Caused by *N. gonorrhea*.
- Clinical features :
 1. Migratory polyarthritis.
 2. Tenosynovitis.
 3. Skin lesions, usually as a small macule or papule on the distal extremities.

2- Lyme disease :

- Lyme disease is caused by spirochaete, *Borrelia burgdorferi*, which is transmitted by ticks.
- Diagnosis : Lyme disease is diagnosed clinically
 - The earliest manifestation of Lyme disease is reddish rash (**erythema migrans**) and flu-like symptoms. Then, In subsequent weeks :
 - Neurologic manifestations : Bell's palsy, meningitis.
 - Cardiac manifestations : AV block, Myopericarditis.
 - Arthritis can develop with knees being the most commonly affected.
 - ELISA test for antibodies to *Borrelia*.

- Treatment :

- ✎ Oral doxycycline 100mg/12h (or amoxicillin if < 8 yrs or pregnant) for arthritis & skin manifestations.
- ✎ Late diagnosed Lyme is treated with intravenous ceftriaxone.

3- **M. Tuberculosis :**

- Spine involvement (Pott's disease) : Back pain, kyphosis, cord compression.
- Peripheral joints : monoarthritis typically involves hip, knee or ankle.

4- **Viral arthritis :**

- Common viruses associated with arthropathy include parvovirus, rubella , HIV & hepatitis B and C .
- Clinical picture : Flu-like symptoms , skin rash & acute polyarthropathy .
- Viral arthritis is usually self limiting.

If you can't explain it simply, you don't understand it well enough.

Albert Einstein

OSTEOPOROSIS

Definition :

- It is the most common metabolic bone disease, characterized by reduced bone density and increased risk of fracture.
- The World Health Organization (WHO) defines osteoporosis as a bone mineral density (BMD) that is 2.5 standard deviations or more below the young adult mean value.

Normal bone	T-score greater than -1
Osteopenia	T-score between -1 and -2.5
Osteoporosis	T-score less than -2.5

Classification :

1- Primary osteoporosis : is subdivided into type 1 and type 2.

- a) Type 1 (postmenopausal osteoporosis) : Most common in women after menopause due to estrogen deficiency. There is high incidence of vertebral fracture.
- b) Type 2 (senile osteoporosis) : occurs in old age and is seen in both females and males at a ratio of 2:1. There is high incidence of hip fracture.

2- Secondary or type 3 osteoporosis : occurs at any age & affects men and women equally due to many causes.

Causes / Risk factors :

- Genetic factor : the single most significant factor.
- Endocrine :
 - ✓ ↓ hormones : Estrogen deficiency in females, hypogonadism in males.
 - ✓ ↑ hormones : Cushing's syndrome, thyrotoxicosis, hyperparathyroidism.
- Drugs : cortisone, heparin, anticonvulsant, chemotherapeutics.
- Malignancy : multiple myeloma, leukemia.
- Inflammatory : rheumatoid arthritis, ulcerative colitis.
- GI : malabsorption, primary biliary cirrhosis.
- Others : Prolonged immobilization, smoking & alcohol intake.

Clinical picture : again, osteoporosis is the most common metabolic bone disease

1. **Asymptomatic** until a fracture occurs, *just radiological osteopenia*.
2. **Pain** : particularly low back pain or neck pain.
3. The most common sites of **fractures** are the forearm (Colles fracture), spine (vertebral fracture) and femur (hip fracture).
4. Kyphosis & abdominal protuberance may follow crushed vertebrae.

Investigations :

I. Laboratory :

- Calcium, phosphate & alkaline phosphatase : are usually normal in primary osteoporosis.
- Investigations of the cause : e.g. cortisol level, thyroid function tests ...

II. Imaging :

- X-ray : may show fractures & osteopenia.
- **Bone mineral density** (BMD) : is measured by DXA (Dual-emission X-ray absorptiometry , previously DEXA).

Treatment :

I. Prevention :

- Diet : adequate dietary calcium & vitamin D intake.
- Weight bearing exercise.
- Avoid smoking & alcohol.
- Correct any secondary cause.

II. Medical treatment :

- Calcium & vitamin D supplements.
- Bisphosphonates e.g. alendronate : anti-resorptive.
- Calcitonin.
- Estrogen replacement therapy : recently estrogen receptor modulators (*Raloxifene*) : act as weak estrogen in some tissues and antagonist in others. No risk of endometrial or breast cancer.
- Recombinant Human Parathyroid Hormone (rhPTH) : it stimulates new bone formation.

OSTEOMALACIA

Definition :

- Osteomalacia is the softening of the bones due to defective bone mineralization secondary to inadequate amounts of phosphorus and calcium. The most common cause is vitamin D deficiency.
- Osteomalacia in children is known as rickets, and because of this, use of the term osteomalacia is often restricted to the adult form of the disease.

Osteomalacia is not the same as osteoporosis. Osteomalacia results from a defect in the bone-building process, while osteoporosis develops due to a weakening of previously constructed bone.

Causes :

The most common cause of the disease is a deficiency in vitamin D, which is normally obtained from the diet and/or sunlight exposure.

1. Dietary deficiency or inadequate sunlight exposure.
2. Malabsorption syndrome.
3. Malnutrition during pregnancy.
4. Chronic metabolic acidosis : Chronic renal failure. Renal tubular acidosis.
5. Abnormal vitamin D metabolism :
 - o Lack of hydroxylation by kidney due to renal disease e.g. CRF.
 - o Long term anticonvulsants e.g. phenytoin : may cause hepatic enzyme induction and increase vitamin D metabolism.
 - o Vitamin D dependent rickets type 1 (VDDR type 1) : an inherited defect in hydroxylase enzyme.
6. End organ resistance to vitamin D : Vitamin D dependent rickets type 2 (VDDR type 2), an autosomal recessive disorder of vitamin D receptors.
7. Hypophosphatemia : *with normal vitamin D*
 - o Familial hypophosphatemic rickets.
 - o Renal Fanconi syndrome : phosphaturia, aminoaciduria, & glycosuria.

Clinical picture :

1. Skeletal discomfort : bone & muscle pain.
2. Proximal myopathy with waddling gait.
3. Pathologic fractures may develop.
4. Manifestations of hypocalcemia : e.g. tetany.
5. *It differs from renal osteodystrophy, where the latter shows hyperphosphatemia.*

Investigations :

- I. Laboratory : (*Biochemical findings*)
 1. The major factor is low vitamin D concentration in blood serum.
 2. The serum calcium is low (*or low normal due to 2^{ry} hyperparathyroidism*)
 3. Serum phosphate is low **except** in cases of renal osteodystrophy.
 4. Serum alkaline phosphatase is high.
- II. **Imaging** : (*Radiological findings*)

Defective mineralization with **pseudofractures** (**Looser's zones**) :

A translucent band of bone material of decreased density may form alongside the surface of the bone. This gives the appearance of a false fracture. Typical sites of involvement are scapula, ribs, pubic rami, proximal ends of the femur and ulna.

Treatment :

- Diet : adequate dietary calcium & vitamin D intake.
- Adequate sun exposure (ultraviolet light).
- Calcium & vitamin D supplements.
- Treatment of the cause.

Comparison of bone pathology

Condition	Calcium	Phosphate	Alkaline phosphatase	Parathyroid hormone	Comments
Osteoporosis	unaffected	unaffected	variable	unaffected	decreased bone mass
Osteomalacia	decreased	decreased	variable	elevated	soft bones
Osteitis fibrosa cystica	elevated	decreased	elevated	elevated	brown tumors
Paget's disease of bone	unaffected	unaffected	variable (depending on stage of disease)	unaffected	abnormal bone architecture

FAMILIAL MEDITERRANEAN FEVER**Definition :**

FMF is an intermittent febrile disorder with inflammatory serositis, arthritis, and rash.

Etiology :

- FMF is a hereditary inflammatory disorder. It is an autoinflammatory disease caused by mutations in the gene MEFV, localized in chromosome 16.
- Eastern Mediterranean persons (especially Arabs, Turks, Greeks, Armenians, and Sephardic Jews) are most frequently affected.

Clinical picture :

- More than 80% of all patients have their first attacks before they are 20 years old. Initial attack is very rare after age 40.
- Most attacks involve fever.
- The attacks last from 6 hours to 3 days, arthritis may last for several weeks. Disease free intervals may last days or months.
- There are 7 types of attacks :
 1. Abdominal attacks affect the whole abdomen with signs of peritonitis, and acute abdominal pain like appendicitis. They occur in 95% of all patients and may lead to unnecessary laparotomy.
 2. Joint attacks mainly occur in large joints, especially in the legs. Usually, only one joint is affected. (75%)
 3. Chest attacks include pleurisy (40 %) and pericarditis (rare).
 4. Scrotal attacks due to inflammation of the tunica vaginalis occurs in up to 5% and may be mistaken for acute scrotum (i.e. testicular torsion).
 5. Myalgia
 6. Erysipelas like rash.
 7. Fever without any of the other symptoms listed above (25%).

Complications :

Amyloidosis with renal failure : amyloid protein is produced in very large quantities during attacks, and at a low rate between them, and accumulates mainly in the kidney, as well as the heart & gastrointestinal tract.

Investigations :

- The diagnosis is clinically made on the basis of the history of typical attacks. No specific test is available to detect familial Mediterranean fever.
- A genetic test : to detect mutations in the *MEFV* gene.
- Markers of inflammation :
 - Leukocytosis, elevated ESR & C-reactive protein levels.
 - Sterile exudative peritoneal or pleural fluid.
- Monitoring the renal function is important especially in patients with a long history of attacks.

Differential Diagnosis :

- Acute appendicitis, rheumatic fever, septic arthritis, systemic juvenile arthritis.
- Pyrexia of unknown origin (PUO).

Treatment :

- Symptomatic relief is the goal of therapy e.g. NSAIDs
- **Colchicine as prophylaxis** (1-2 mg/d) : It reduces the frequency of attacks, protect against amyloidosis & stabilizes the proteinuria.
- If the symptoms are not controlled by colchicine, then alpha-interferon, infliximab or anakinra may be recommended.
- Corticosteroids are ineffective.

We think so because all other people think so, or...because we were told to think so, and think we must think so...

RUDYARD KIPLING

SARCOIDOSIS

Definition :

Sarcoidosis is a multisystem granulomatous disorder of unknown etiology, most commonly affecting young adults. Granulomas most often appear in the lungs or the lymph nodes, but any organ can be affected.

Pathology :

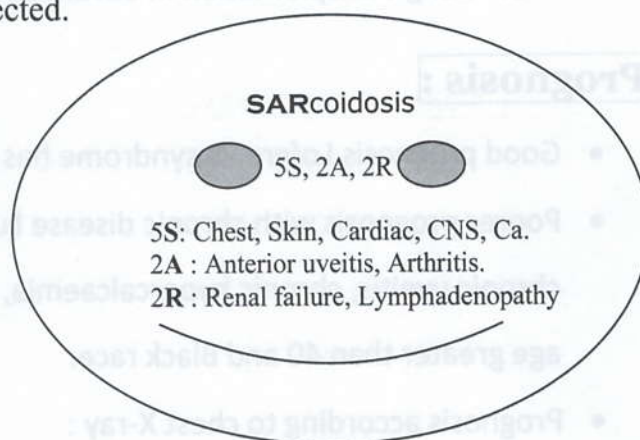
The characteristic granuloma composed of macrophages, lymphocytes with intracellular inclusion bodies.

Etiology :

- The exact cause of sarcoidosis is not known.
- Most probably due to alteration in immune response after exposure to antigenic stimulus (an environmental, occupational, or infectious agent).

Clinical picture :

1. It may be asymptomatic.
2. Pulmonary : dyspnea, cough, wheezing , may be hemoptysis.
3. Upper airway : nasal obstruction, hoarseness of voice.
4. Lymphadenopathy : painless, rubbery LN enlargement. The cervical & scalene lymph nodes are most frequently affected.
5. Skin :
 - Erythema nodosum (*red painful bumps on the anterior aspect of the leg*)
 - Lupus pernio : violaceous lesions on the nose & cheeks.
6. Eye : Anterior uveitis.
7. Joints : Polyarthritis.
8. Cardiac : Arrhythmia, congestive heart failure.
9. CNS : cranial neuropathy (*facial nerve most often affected*), diabetes insipidus.



10. Renal : ARF can be due to hypercalcemia & granulomatous interstitial nephritis.
11. Hypercalcemia : due to excess production of vitamin D.

Investigations :

Chest X-ray :

Stage I	Bilateral hilar lymphadenopathy
Stage II	Bilateral hilar lymphadenopathy and pulmonary infiltration
Stage III	Pulmonary infiltration only
Stage IV	Fibrosis.

- The combination of bilateral hilar lymphadenopathy , erythema nodosum in association with fever & arthralgia is known as Lofgren syndrome.
- The main differential diagnosis are TB & lymphoma, and every effort should be made to confirm the diagnosis of sarcoidosis histologically (Lung ,LN or skin biopsy)

Treatment :

1. Cortisone is the main therapy.
2. Others : methotrexate, chloroquine.
3. Lung transplantation in advanced cases.

Prognosis :

- Good prognosis Lofgren's syndrome has complete resolution in 80% of people.
- Poorer prognosis with chronic disease Lupus pernio, nasal mucosa involvement, chronic uveitis, chronic hypercalcaemia, nephrocalcinosis, neural involvement, age greater than 40 and Black race.
- Prognosis according to chest X-ray :
 - ✓ Stage II : 50% cases recover spontaneously in 2 years, 30 - 40% require systemic steroids, 10 - 15% require long-term steroids.

Stage III : Worse prognosis. Only 30% show significant improvement with

LOW BACK PAIN (LBP)

Low back pain is a common musculoskeletal disorder. *Nearly everyone has low back pain sometime.*

Etiology :

1. Mechanical :

- Lumber disc prolapse.
- Lumbar spondylosis.
- Lumbar spinal stenosis : is a medical condition in which the spinal canal narrows and compresses the spinal cord and nerves at the level of the lumbar vertebra. This is usually due to spinal degeneration that occurs with aging.
- Osteoarthritis.
- Fractures.
- Bad posture (sitting, standing).
- Leg length difference.
- Congenital : Scoliosis.

2. Inflammatory :

- Seronegative spondylarthritides (e.g. ankylosing spondylitis).
- Rheumatoid arthritis.

3. Infection :

- Osteomyelitis.
- Pott's disease (TB)

4. Neoplastic :

- Bone tumors (primary or metastatic).
- Intradural spinal tumors.

5. Metabolic :

- Osteoporosis.
- Osteomalacia.
- Paget's disease.

6. Referred :

- Peptic ulcer.
- Pancreatitis.
- Pyelonephritis.
- Prostate cancer.

7. Psychogenic low back pain.

- The intervertebral disc is formed of a central gelatinous part " nucleus pulposus ", surrounded by a fibrous tissue ring " annulus fibrosus " and covered from above & below by a cartilaginous plate.
- **Acute disc prolapse** : sudden rupture of the annulus fibrosis followed by bulging (herniation) of the nucleus pulposus. This compresses the spinal roots. It may occur at any age due to trauma e.g. lifting heavy objects or jumping to the floor from a height.
- **Spondylosis** : It is a gradual, progressive degeneration of the intervertebral discs, specially freely mobile discs e.g. cervical & lumbar regions, leading to herniation of the nucleus pulposus.

Diagnostic approach :**I. History** : e.g.

- Mechanical causes : pain radiating to buttocks or thighs. Only true sciatica from nerve root compression radiates below the knee to the foot.
- A history of low back pain with morning stiffness in a younger patient raises the question of ankylosing spondylitis.
- Spinal stenosis : often presents with back or leg pain that worsens with walking (pseudoclaudication) and with prolonged standing and relieved with sitting in flexion.

II. Examination :

- Back signs : tenderness, deformity
- **Signs of nerve root compression** : See neurology, and you may understand ☺

Disc herniation (e.g. Lumbar disc prolapse) occurs at the L4-L5 level or L5-S1 level in 95% of all disc herniation :

1. Motor manifestations : Weakness of dorsiflexion occurs in L5 root compression, and weakness of plantar flexion occurs in S1 root compression.
2. Sensory examination in these patients may reveal saddle anesthesia (decreased sensation over buttocks, perineum and posterior thighs).
3. Bladder dysfunction.
4. Straight leg raising test : positive sign indicates sciatica.

Differentiating features between mechanical & inflammatory LBP :

	Mechanical	Inflammatory
Example	Disc prolapse	Ankylosing spondylitis
Onset	Acute	Gradual
Age	Any age	Usually < 35
Effects of exercise	Worse	Better
Morning stiffness	+	+++
Spinal tenderness	Localized, Usually L4, L5, S1	Diffuse
Motor, sensory, bladder manifestations	+	-
Scoliosis	+	-
Other system is involved	-	+
Sacroiliac / Hip involvement	-	+

III. Investigations :

- X-ray, CT, MRI & Myelography : in the cases where "red flags" are present e.g.
 - ✖ Recent significant trauma.
 - ✖ Unexplained weight loss or fever.
 - ✖ Previous or current cancer.
 - ✖ Osteoporosis or chronic corticosteroid use.
 - ✖ Age greater than 70 years.
 - ✖ Focal neurological deficit.
 - ✖ Duration greater than 6 weeks.

Treatment of mechanical LBP :**I. Instruction :** (patients education)

1. Rest.
2. Position :
 - Avoid prolonged standing.
 - Sleeping on medium firm mattresses.
3. Avoid lifting heavy object while unsupported back especially in disc prolapse.
4. Weight reduction.

II. Medical treatment :

- ✖ NSAIDs during acute attacks.
- ✖ Muscle relaxants.

III. Local measures :

1. Physical agents : heat, ice, massage, ultrasound, and electrical stimulation.
 - Local anti-inflammatory effect.
 - Decrease pain & muscle spasm.
 - Decrease fibrosis & adhesion.
2. Exercise program : e.g. flexion exercise (abdominal exercise).

IV. Surgical treatment : e.g. microdiscectomy, laminectomy or spinal fusion.**- Indications :**

- Failure of conservative treatment in reducing pain.
- Progressive neurologic symptoms e.g. leg weakness, bladder disturbances.

COLLECTIONS OF RHEUMATOLOGY

DD of neck pain	DD of back pain
I- Mechanical • Trauma. • Cervical spondylosis. • Disc prolapse. • Muscle spasm.	I- Mechanical • trauma. • Lumbar spondylosis. • Disc prolapse. • Muscle spasm.
II- Inflammatory: • Sero-ve arthropathy. • Rheumatoid arthritis.	II- Inflammatory: • sero -ve arthropathy. • <u>Brucellosis</u>. MCQ
III- Metabolic: • Osteoporosis. • Osteomalacia.	III- Metabolic: • Osteoporosis. • Osteomalacia.
IV- Neoplasm: • Metastasis • M. Myeloma • Lymphoma	IV- Neoplasm: • Metastasis • M. Myeloma • Lymphoma
V- Referred Pain: - Angina - Pancost tumor - Aortic aneurysm	V- Referred Pain: - Pancreatitis, Peptic ulcer - Cancer pancreas - MI – Renal colic - Prostate or cervix disease.

DD of non inflammatory arthritis:

- Trauma.
- Osteoarthritis.
- Hemoartherosclerosis (hemophilia).
- Charcot joint.

DD of inflammatory arthritis:

- Rheumatoid arthritis.
- Septic arthritis.
- SLE
- Sero -ve arthropathy.
- Gout
- Pseudo gout.

How can you differentiate between inflammatory & non inflammatory arthropathy ?**Inflammatory :**

- ☞ Pain (↓ by exercise & ↑ by rest).
- ☞ Morning stiffness.
- ☞ ESR, CRP : ↑↑
- ☞ Extra-articular manifestations.

Non-inflammatory :

- ☞ Pain (↑ by exercise & ↓ by rest)
- ☞ Normal laboratory finding.
- ☞ No systemic manifestations.

DD of polyarthropathy :**1. Causes of chronic polyarthritis : (> 6 weeks)**

- Rheumatoid arthritis.
- SLE.
- Systemic sclerosis.
- Sero -ve arthropathy e.g. Reiter's syndrome, Psoriatic arthropathy.
- Sarcoidosis.
- Chronic gout.
- Osteoarthritis.
- Vasculitis.

2. Causes of acute polyarthritis :

- Acute rheumatic fever.
- Bacterial endocarditis.
- Rheumatoid arthritis. (10 % of cases)
- SLE.
- Reiter's syndrome, psoriatic arthritis.
- Viral infection : rubella, hepatitis B, HIV, Epstein-Barr.

Differential diagnosis of rheumatoid arthritis = DD of polyarthropathy

History & examination are often helpful in narrowing the differential diagnosis e.g.

SLE :

- May have the similar distribution of joint involvement but rarely erosive.
- Clinical manifestations & serological finding :

Sero-ve spondylopathy :

- Asymmetrical joint involvement.
- Central joints > peripheral joints.
- RF : -ve

Osteoarthritis :

- Absence of systemic inflammatory manifestations
- Onset in later life.
- Pain : ↑ by exercise , ↓ by rest.
- Common joints involved are : Knee, thumb base, Hips
- Normal lab finding & normal ESR.

Chronic gout :

- Clinical manifestations :
- Investigations :

Viral infections :

- May result in a polyarthritis clinically mimic RA.
- Skin rash, self limited course.
- It is important to exclude chronic hepatitis & HIV.

DD of monoarthritis:

- Rheumatic fever.
- Acute gout.
- Pseudogout.
- Septic arthritis.
- Traumatic hemoarthrosis..
- Atypical rheumatoid arthritis.

Acute septic arthritis	<i>Suggested by:</i> extremely painful, hot red joint, high fever.
	<i>Confirmed by:</i> Joint aspiration: ↑ neutrophils. Culture : +ve e.g. staphylococci or streptococci or pseudomonas or gonococci or TB, etc.
Gout	<i>Suggested by:</i> one acutely inflamed joint (usually small esp. big toe) at a time, but other joints in hands, arms, legs, and feet deformed. Tophi on ears and tendon sheaths.
	<i>Confirmed by:</i> ↑ serum urate (not always). Urate crystals (negatively birefringent in plane-polarised light) present on joint aspiration .
Pseudogout (Ca pyrophosphate arthropathy, chondrocalcinosis)	<i>Suggested by:</i> one painful joint (usually knee) especially in elderly <i>or</i> history of hyperparathyroidism <i>or</i> myxedema <i>or</i> osteoarthritis <i>or</i> hemochromatosis <i>or</i> acromegaly.
	<i>Confirmed by:</i> joint aspiration: Ca-pyrophosphate crystals in synovial fluid
Rheumatic fever	<i>In fact, rheumatic fever is flitting polyarthritis.</i> Diagnostic criteria :
Traumatic hemarthrosis	<i>Suggested by:</i> acutely inflamed joint after trauma.
	<i>Confirmed by:</i> joint aspiration: aspiration of blood from joint.
Rheumatoid arthritis	<i>Suggested by:</i> morning stiffness , Articular manifestations : (.....) & Extra-articular : e.g. palmar arythema , amyloidosis
	<i>Confirmed by:</i> +ve rheumatoid factor, Anti CCP , <i>characteristic X-ray.</i>
Leukemic joint deposits	<i>Suggested by:</i> acutely inflamed joint.
	<i>Confirmed by:</i> leukemic picture on peripheral film and bone marrow .
Reactive arthritis	<i>Suggested by:</i> asymmetric mono- or oligoarthritis developing about 1 week after infection elsewhere.
	<i>Confirmed by:</i> Lab evidence of venereal or enteric infection, <i>Yersinia, Chlamydia trachomatis, Salmonella/Shigella and Chl. Pneumonia.</i>

Causes of knee pain :**I. Intraarticular :**

- Inflammatory : RA, sero-ve arthropathy, pseudogout
- Septic arthritis.
- Osteoarthritis.

II. Extraarticular : Fractures, tumors, trauma, tendonitis.**III. Referred pain : Hip, lumbosacral spine.****DD of recurrent arthritis:**

- Rheumatic fever
- Pseudogout
- Sero-ve arthropathy.
- Gout
- Rheumatoid arthritis.

DD of Symmetric arthritis:

- Rheumatoid arthritis.
- SLE.
- Hepatitis B

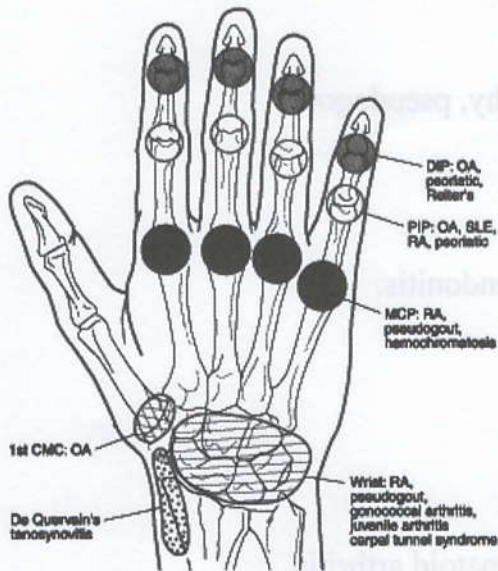
What are 3 principal crystals associated with joint inflammation ?

- Urate : Gout.
- Calcium pyrophosphate : Pseudogout.
- Hydroxyapatite : Pseudo-pseudogout.

**MCQ****Drug induced rheumatic diseases :**

- **Arthralgia:** quindine, quinolones, cimitidine, interferon, amphotericine B
- **Myalgia/Myopathy** : glucocorticoids, Penicillamine, chloroquine, statins, quinolones, interferon, alcohol.
- **Gout** : diuretics, aspirin, alcohol.
- **SLE** : hydralazine, INH, Penicillamine, phenytoin.
- **Scleroderma** : carbidopa , tryptophan.
- **Vasculitis** : allopurinol , amphetamine , thiazide, penicillamine.

Arthritis of small joints of the hand :



- 1- **DIP** : OA , Psoriatic , Reiter's .
- 2- **PIP** : OA , Psoriatic , SLE , RA .
- 3- **MCP** : RA , Pseudogout , hemochromatosis
- 4- **1st CMC** : OA
- 5- **wrist** : RA, Pseudogout , gonococcal arthritis
Carpal tunnel syndrome
Juvenile arthritis.

DIP : distal interphalangeal

PIP : proximal interphalangeal

MCP : metacarpophalangeal

CMC : carpometacarpal .

Causes of purpura in a patient with connective tissue disease :

- 1- Vasculitis .
- 2- Cortisone therapy.
- 3- Thrombocytopenia due to NSAIDs.
- 4- Amyloidosis.
- 5- Factor VIII antibodies (SLE, RA).

What are the physical finding in carpal tunnel syndrome:

- 1- Wasting of the thenar eminence.
- 2- Weakness of the thumb .
- 3- Sensory loss of the first 3 fingers & half of the ring finger
- 4- Numbness & pain reproduced by flexion of the wrist for one minute.
- 5- Features of the cause : **DM**, **RA**, **A**crromegaly , **M**yxedema. (Dr. Ahmed Mowafy ☺)

Risk factors of amyloidosis :

- Age : > 50
- Chronic infection or inflammatory disease as RA , **FMF**
- Family history.
- Multiple myeloma , Hodgkin's disease.
- Kidney disease that has required dialysis for more than 5 years.

DD of arthritis associated with subcutaneous nodules :

- 1- Rheumatic fever.
- 2- Rheumatoid arthritis.
- 3- Gout.
- 4- Still's disease.

DD of arthropathy :

Acute	Chronic
I- Infection: ➤ Bacterial: ○ <i>N. gonorrhoeae</i> ○ <i>Staph aureus</i> ○ Streptococci ○ Gram-ve bacilli : Brucella ➤ Viral : ○ Rubella ○ Hepatitis B,C	I- Infection: ○ TB ○ Syphilis ○ Chronic septic arthritis .
II- Immune: ○ Rheumatic fever . ○ Rheumatoid arthritis. ○ Vasculitis.	II- Immune: ○ All collagen diseases .
III- Metabolic: ○ Acute gouty arthritis. ○ Pseudogout	III- Metabolic: ○ Chronic gouty arthritis. ○ Pseudogout. ○ Amyloidosis ○ Haemochromatosis
IV- Degenerative : -----	IV- Degenerative: ○ Osteoarthritis.
V- Endocrinal: -----	V- Endocrinal: ○ Acromegaly. ○ Myxedema.
VI-Miscellaneous: ○ Traumatic arthritis. ○ Hemarthrosis (hemophilia)	VI - Miscellaneous: ○ Charcot's joint: occurs in DM, Tabes dorsalis ○ Sarcoidosis.

Differentiate between rheumatic & rheumatoid arthritis :

	Rheumatic fever	Rheumatoid arthritis
Etiology	Post-streptococcal pharyngitis	Autoimmune disease
Coarse	< 6 weeks	> 6 weeks
Articular manifestations	Big joints Not erosive	Small joints. Erosive
Extra-articular manifestations		
Investigations		
Treatment	✗ Penicillin for pharyngitis ✗ Aspirin for Arthritis. ✗ Cortisone for Carditis.	

Differentiate between Reiter's & Behcet's syndrome :

	Reiter's syndrome	Behcet's syndrome
Male : Female ratio	10 - 1	2 - 1
Ulcers	Painless	Painful
Eye	Conjunctivitis	Uveitis
Spondylitis & Sacroilitis	Frequent	Uncommon
HLA	B27	B27, B5
Role of infection	Play a big role	No role
Treatment	NSAIDs	Immunosuppressive

Rheumatology MCQ

1- A 64 years old man presents with a vasculitic skin rash , a peripheral neuropathy and gastrointestinal blood loss. He is found to have proteinuria on dipstick urinalysis. Which one of the following is the most likely diagnosis ?

- A) Microscopic polyangiitis.
- B) Wegener's granulomatosis.
- C) Henoch-Schonlein vasculitis.
- D) Polyarteritis nodosa.
- E) Churg-Struss syndrome.

2- A 62 year old man complains of pain around the first metatarsophalangeal joint of the left foot. He is otherwise well and is not on any medication. Which one of the following is correct?

- A) A raised uric acid level would confirm a diagnosis of gout.
- B) Allopurinol should be commenced during the attack.
- C) Osteoarthritis is the most likely diagnosis.
- D) A normal uric acid exclude a diagnosis of gout.
- E) Presence of chondrocalcinosis would confirm a diagnosis of pseudogout.

3- Which of the following statements regarding drug induced lupus (DIL) is not true?

- A) Central nervous system and renal involvement is uncommon in DIL.
- B) Classical lupus skin findings are uncommon in DIL.
- C) Drugs implicated in the etiology of DIL should not be used in idiopathic SLE.
- D) Methyldopa is implicated in causing DIL.
- E) More than 50% of patients taking procainamide for more than 12 months develop +ve ANA titres.

4- Which one of the following is a feature of aggressive disease in rheumatoid arthritis ?

- A) All of the options.
- B) Functional disability.
- C) High rheumatoid factor titre.
- D) Raised C reactive protein.
- E) Rheumatoid nodules.

5- A 58 year-old man presents with blurred vision, an occipital headache, fatigue and shoulder girdle pain. On examination he has scalp tenderness, myalgia but no myopathy, and no evidence of fundoscopic or neurological abnormality. Which one of the following would be the correct immediate action?

- A) Commence a NSAID.
- B) Commence oral prednisolone at 20 mg/d.
- C) Request an ESR and temporal artery biopsy.
- D) Request CT scan of the head.
- E) Start the patient on 60 mg/d oral prednisolone.

6- You are investigating a patient with glomerulonephritis. A renal biopsy tissue specimen was reported as, "there are no immune deposits on immunohistochemical analysis" This is characteristic of which one of the following renal disorders?

- A) SLE.
- B) Henoch Schonlein nephritis.
- C) Goodpasture's syndrome.
- D) Wegener's granulomatosis.
- E) Buerger's disease.

7- Which of the following types of arthritis is the most common type of psoriatic arthropathy?

- A) Distal interphalangeal (DIP) joint disease.
- B) Arthritis mutilans.
- C) Peripheral symmetrical polyarthropathy.
- D) Peripheral asymmetrical oligoarthropathy.
- E) Psoriatic spondylitis.

8- Which one of the following would be characteristic of the laboratory findings in a patient with antiphospholipid syndrome?

- A) Low C3 and C4 concentrations.
- B) Positive anticardiolipin antibodies.
- C) Prolonged INR.
- D) Elevated LDL.
- E) Thrombocytosis.

9- Which of the following is often associated with low uric acid levels ?

- A) Thiazide diuretic therapy.
- B) Alcoholism.
- C) Polycythemia rubra vera.
- D) Eclampsia of pregnancy.
- E) Psoriasis.

10- A 58 year old women who has had Sjogran's syndrome for ten years presents with enlarged cervical lymph nodes. Which one of the following is the most likely neoplasm responsible for this presentation?

- A) Gastric carcinoma.
- B) Lymphoma.
- C) Bronchial carcinoma.
- D) Chronic lymphatic leukemia.
- E) Pancreatic adenocarcinoma.

11- The following diseases are associated with antinuclear and rheumatoid factor EXCEPT :

- A) Infective endocarditis.
- B) Autoimmune thyroiditis.
- C) Sjogren's syndrome.
- D) Fibrosing alveolitis.
- E) Ankylosing spondylitis.

12- Presentation with acute monoarthritis suggests the possibility of EXCEPT

- A) Crystal arthritis.
- B) Trauma.
- C) Bacterial infection.
- D) Rheumatoid arthritis.
- E) Hemochromatosis.

13- One of the following suggests a mechanical rather than inflammatory cause of back pain :

- A) Back pain and stiffness exacerbated by resting.
- B) An elevated C reactive protein.
- C) +ve rheumatoid factor.
- D) Gradual mode of onset in an elderly patient.
- E) Radiation of pain down the back of one leg to the ankle.

14- The typical features of rheumatoid arthritis include :

- A) Onset usually before the age of 30 years.
- B) Male to female ratio of 3 : 1
- C) Sparing of joints of the pelvic and shoulder girdle.
- D) Association with HLA-DR4
- E) No progression to bone & cartilage destruction.

15- Criteria for the diagnosis of rheumatoid arthritis include : EXCEPT

- A) Morning stiffness lasting more than 1 hour.
- B) Arthritis in both hip joints.
- C) The presence of rheumatoid nodules.
- D) Symmetrical polyarthritis.
- E) Positive rheumatoid factor.

16- Typical features of active rheumatoid arthritis include :

- A) Fever and weight loss.
- B) Macrocytic anemia.
- C) Anterior uveitis.
- D) Thrombocytopenia.
- E) Polycythemia.

17- The following statements about rheumatoid arthritis are true EXCEPT :

- A) joint pain and stiffness is typically aggravated by rest.
- B) the rheumatoid factor test is positive in about 70% of patients.
- C) joint involvement is additive rather than flitting.
- D) associated scleromalacia typically produce painful red eyes.
- E) symmetrical peripheral joint involvement.

18- Diseases associated with seronegative spondylopathy include EXCEPT :

- A) Still disease.
- B) Whipple's disease.
- C) Sjogran's disease.
- D) ulcerative colitis.
- E) Behcet's disease.

19- The features of classical polyarthritis nodosa include EXCEPT :

- A) more common in males.
- B) an association with circulating immune complexes containing hepatitis B virus.
- C) involvement of small arteries and arterioles.
- D) multiple peripheral nerve palsies.
- E) severe hypertension.

20- A 70 year-old man complains of painful joints in his hips and knees , which you have diagnosed as osteoarthritis. Which of the following is the best agent to prescribe for this patient?

- A) Naproxen sodium.
- B) Celecoxib
- C) Oral prednisone.
- D) Intraarticular prednisone.
- E) Paracetamol.

Match the following diseases (A-E) to the clinical setting described in questions (21-23)

- A) Gonococcal arthritis.
- B) Gout.
- C) SLE.
- D) Osteoarthritis.
- E) Rheumatoid arthritis.

21- Symmetrical bilateral ulnar deviation of both hands in a 42-year-old woman.

22- Painful ,swollen metatarsophalangeal great toe (unilateral) with redness and warmth after dinner in a 45-year-old.

23- Unilateral non tender bony enlargement of first DIP and activity related right hip pain in a 66 year old woman.

24- Overdoses of salicylates lead to all of the following EXCEPT :

- A) Nausea and vomiting.
- B) Tinnitus.
- C) Marked hyperventilation.
- D) Increased metabolic rate.
- E) Increase in blood PH.

25- Rheumatoid factor in SLE is positive in :

- a. 20 %
- b. 35 %
- c. 50 %
- d. 70 %

26- Which is the specific antibody for SLE

- a. Anti Ro/La
- b. Anti-RNP
- c. Anti-ss DNA
- d. Anti-Sm

27- Extra-articular manifestations of rheumatoid arthritis include EXCEPT

- a. Cutaneous ulceration
- b. Pericardial & pleural effusion
- c. Amyloidosis
- d. Anterior uveitis

28- ANA in SLE is positive in approximately

- a. 60 %
- b. 75 %
- c. 80 %
- d. 95 %

29- Which is NOT used to treat acute gouty arthritis

- a. Etoricoxib
- b. Allopurinol
- c. Colchicine
- d. Prednisolone

30- Which is NOT regarded as a small vessel vasculitis

- a. Microscopic polyangiitis
- b. Henoch-Schonlein purpura
- c. Polyarteritis nodosa
- d. Essential mixed cryoglobulinemia.

31- Which of the following usually presents as monoarthropathy

- a. SLE
- b. Rheumatoid arthritis
- c. Gout
- d. Sjogren's syndrome

32- Metacarpophalangeal joints are usually NOT affected in

- a. Osteoarthritis
- b. Rheumatoid arthritis
- c. Ankylosing spondylitis
- d. Reactive arthritis

33- Brucella arthritis commonly affects

- a. Knee joint
- b. Joints of hands
- c. Spine
- d. Metatarsophalangeal joint

34- CREST syndrome is aggregation of Calcinosis , Raynaud's , Sclerodactyly, Telangiectasia and

- a. Edema
- b. Esophageal hypomotility
- c. Endomyocardial fibrosis
- d. Exophthalmos

35- Felty's syndrome doesn't include :

- a. Rheumatoid arthritis.
- b. Splenomegally.
- c. Hepatomegally.
- d. Pancytopenia.

36- CREST syndrome is diagnosed by presence of

- a. Anti-RNP antibody
- b. Anti-centromere antibody
- c. Anti-Jo-1 antibody
- d. Anti-histone antibody

37- Which is false as regard to ARA criteria of rheumatoid arthritis

- a. Rheumatoid nodules
- b. Morning stiffness > 1 hour
- c. Asymmetrical arthritis
- d. Arthritis of hand joints

38- In rheumatoid arthritis , rheumatoid factor is formed against

- a. IgG
- b. IgM
- c. IgA
- d. IgD

39- Commonest metabolic bone disease is

- a. Osteoarthritis
- b. Rickets
- c. Osteoporosis
- d. Osteomalacia

40- Recurrent anterior uveitis is most characteristic of

- a. Behcet's syndrome
- b. SLE
- c. Rheumatoid arthritis
- d. Sjogren's syndrome

41- Hydroxychloroquine toxicity does not produce

- a. Maculopathy
- b. Corneal deposits
- c. Optic atrophy
- d. Cataract

42- Rheumatoid arthritis is strongly associated with HLA

- a. DR3
- b. DR4
- c. B27
- d. B8

43 - A 22 years woman has repeated attacks of myalgia , arthralgia , pericarditis and pleural effusion for few years. The laboratory screening test should be

- a. Rose Waaler agglutination test
- b. ANA
- c. ASO titre
- d. CD4 lymphocyte count.

44 - Esophagus is most commonly involved by

- a. Progressive systemic sclerosis
- b. Polymyositis
- c. Polyarteritis nodosa
- d. Behcet's syndrome

45- The dose of methotrexate in treatment of rheumatoid arthritis :

- a. 200 – 400 mg/day
- b. 200 – 400 mg/week
- c. 7.5 mg/day
- d. 7.5 mg/week

46- HLA B27 tissue typing is NOT associated with

- a. Psoriatic arthropathy
- b. Ankylosing spondylitis
- c. Reiter's syndrome
- d. Behcet's syndrome

47- The most common rheumatological disease is :

- a. Osteoarthritis
- b. Rheumatoid arthritis.
- c. Gout
- d. SLE

48- Drug induced SLE is NOT commonly associated with

- a. Polyarthrits
- b. Pulmonary infiltrates
- c. Renal involvement
- d. Polyserositis

49- Bouchard's node in osteoarthritis is seen in

- a. Carpo-metacarpal joint
- b. Metacarpo-phalangeal joint
- c. Proximal interphalangeal joint
- d. Distal interphalangeal joint

50- Rheumatoid nodules are characterized by all EXCEPT

- a. Big
- b. Tender
- c. Fixed to skin
- d. Ulcerate

51- Ocular manifestations of rheumatoid arthritis usually do not include

- a. Anterior uveitis
- b. Episcleritis
- c. Scleromalacia
- d. Keratoconjunctivitis sicca

52- Drug of choice for relieving pain in osteoarthritis is

- a. Cortisone
- b. Ibuprofen
- c. Paracetamol
- d. Diclofenac

53- Pseudogout is associated with deposition of crystals of

- a. Calcium oxalate
- b. Calcium phosphate
- c. Calcium pyrophosphate dehydrate
- d. Monosodium urate

54- All of the following indicate poor prognosis in rheumatoid arthritis EXCEPT

- a. High titre of rheumatoid factor
- b. Extra-articular manifestations
- c. Acute onset of disease
- d. Early development of nodules.

55- In Churg-Struss syndrome , the principle organ involved is

- a. Lung
- b. Kidney
- c. Central nervous system
- d. Liver

56- Kawasaki disease is associated with

- a. Coronary artery aneurysm
- b. Renal failure
- c. Pleural effusion
- d. Polyarteritis nodosa

57- Which organ is NOT included in classic Wegner's granulomatosis

- a. Lung
- b. Kidney
- c. Heart
- d. Nose

58- c-ANCA is diagnostic of

- a. Polyarteritis nodosa
- b. Microscopic polyarteritis
- c. Wegner's granulomatosis
- d. Crescentic GN

59- HBsAg is present in vasculitis associated with

- a. Henoch-Schonlein purpura
- b. Temporal arteritis
- c. Churg-Struss syndrome
- d. Polyarteritis nodosa

60- Colchicine may be used in all EXCEPT

- a. Scleroderma
- b. Chronic gout
- c. Myelofibrosis
- d. Primary biliary cirrhosis.

61- The diagnostic criteria for SLE includes all of the following EXCEPT

- a. Raynaud's phenomena
- b. Hemolytic anemia
- c. Alopecia
- d. Positive ANA

62- Boutonniere deformity is

- a. Extended distal & flexed proximal interphalangeal joints
- b. Flexed distal & extended proximal interphalangeal joints
- c. Flexed distal & proximal interphalangeal joints
- d. Extended distal & proximal interphalangeal joint

63 - Highest incidence of rheumatoid factor is found in

- a. SLE
- b. Rheumatoid arthritis
- c. Sjogren's syndrome
- d. Progressive systemic sclerosis.

The answers

1- D : Polyarteritis nodosa.

Wegner's can affect the eyes , ENT and upper respiratory tract ,lower respiratory tract and kidneys,and involve the peripheral or central nervous system .However vasculitis involving the GIT is uncommon. Microscopic polyangiitis primarily affects the kidney, and Churg Struss syndrome is associated with atopy , peripheral neuropathy, esinophilia and fleeting pulmonary granuloma. Both Henoch Schonlein vasculitis & PAN can involve GIT , kidneys and skin but PAN is more commonly associated with a peripheral neuropathy . Henoch Schonlein vasculitis can occur in adults but is much commoner in children.

2- C) Osteoarthritis is the most likely diagnosis.

Hyperuricemia is ten times more commoner than gout and uric acid levels can be normal during a flare-up of gout. Hence ,uric acid can neither confirm nor exclude a diagnosis of gout in this case where joint pain is current. Similarly chondrocalcinosis (presence of calcium in joint) is much more common than pseudogout and the commonest joints involved are the knees, wrists and index metacarpal joints (hemochromatosis) . OA commonly affects the first MTP joints and, until the diagnosis is confirmed , treatment with allopurinol should not be commenced . In the absence of a +ve family history , a history of alcohol intake or other medication, OA is more likely than gout.

3- C) Drugs implicated in the etiology of DIL should not be used in idiopathic SLE.

Many drugs have been implicated in causing drug induced lupus such as hydralazine, procainamide , INH , methyldopa . Up to 90% of patients taking procainamide develop a +ve ANA and 30% of these develop DIL.

Renal, CNS & skin features of SLE are rare in DIL.

In the majority of cases the condition subsides on withdrawing the drug.

There is no contraindication to using these drugs in idiopathic SLE.

4- A) All of the options.

5- E) Start the patient on 60 mg/d oral prednisolone.

Temporal arteritis , often associated with polymyalgia rheumatic, tends to occur abruptly and is commonly associated with either a temporal or occipital headache, scalp tenderness , jaw claudications , and visual disturbance . In the presence of latter, high dose oral prednisolone should be commenced immediately to try and prevent visual loss from ischemic optic neuropathy . A high ESR and histological evidence of arteritis are useful diagnostic tests. Although a biopsy is best performed as early as possible , the introduction of prednisolone should never be delayed.

6- D) Wegener's granulomatosis.

Wegener's granulomatosis is a primary small vessel vasculitis which involves the kidneys and causes glomerulonephritis with crescent formation. It is distinguished from other causes of glomerulonephritis by the absence of immune deposits on immunohistochemical analysis.

7- D) Peripheral asymmetrical oligoarthritis.

Peripheral oligoarthritis is the most common presentation of psoriatic arthritis and accounts for 40% of all cases. It usually presents with an asymmetrical pattern of large and small joint involvement. Symmetrical polyarthritis resembling rheumatoid arthritis may occur in 20 % of patients. Psoriatic spondylitis accounts for 20% of cases. Synovitis of DIP joints of the hands is almost pathognomonic of psoriatic arthritis but occurs in less than 10% of all cases.

8- B) Positive anticardiolipin antibodies.

Antiphospholipid syndrome is characterized by **thrombosis** of arteries and veins , recurrent abortions and **thrombocytopenia** in association with laboratory finding of antibodies directed against phospholipid .(These antibodies can be specific such as **anticardiolipin antibodies**). Also **prolonged aPTT** & although there is an increased risk of atherosclerosis and ischemic heart disease , elevated LDL is not a feature of the primary condition. Complement levels are generally normal in this disorder.

9- D) Eclampsia of pregnancy.

10- B) Lymphoma.

11- E) Ankylosing spondylitis.

12- D) Rheumatoid arthritis.

13- E) Radiation of pain down the back of one leg to the ankle.

Suggests lumbar nerve root compression

14- D) Association with HLA-DR4

In rheumatoid arthritis no age group is exempt. The male : female ratio is 1 : 3 .
There is sparing of **DIP** joints.

15- B) Arthritis in both hip joints.

16- A) Fever and weight loss.

17- D) associated scleromalacia typically produce painful red eyes.

Scleromalacia is a painless wasting of the sclera unlike the rarer scleritis.

18- C) Sjogran's disease.

19- C) involvement of small arteries and arterioles.

Systemic vasculitis affecting medium sized arteries.

20- E) **paracetamol** , It is the first agent of choice in the treatment of early osteoarthritis.

21- E

22- B

23- D

24- E) **Increase in blood PH.** Overdose of salicylates causes acidosis.

- | | |
|-------|----------------------|
| 25- a | 44- a |
| 26- d | 45- d |
| 27- d | 46- d |
| 28- d | 47- a |
| 29- b | 48- c |
| 30- c | 49- c |
| 31- c | 50- b |
| 32- a | 51- a |
| 33- c | 52- c |
| 34- b | 53- c |
| 35- c | 54- c |
| 36- b | 55- a |
| 37- c | 56- a |
| 38- a | 57- c |
| 39- c | 58- c |
| 40- a | 59- d |
| 41- d | 60- b |
| 42- b | 61- a SLICC criteria |
| 43- b | 62- a |
| 63- c | |

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